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EARLY PREMATURE INFANT PHYSIOLOGIC AND BEHAVIORAL INDICATORS OF ANS INSTABILITY

by

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Submitted in Partial Fulfillment of the Requirements

For the Degree of Doctorate of Philosophy in

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College of Nursing

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DEDICATION

I dedicate this dissertation to the babies and families I have been so honored to gently care for during their journey in Neonatal Intensive Care Units.

ACKNOWLEDGEMENTS

I acknowledge my family and friends who provided unwavering support to me during my three-year journey. You provided love, patience, and encouragement for which I am very grateful for. Thank you, to my husband Dave, my daughters Katie and Lauren, and my dearest friend Beth, for your continued encouragement and unending love.

It has been my honor to have been surrounded by an expert dissertation committee and the UofSC College of Nursing Faculty. Dr. Robin Dail inspired learning and a deep passion for exploration to unknown questions. As Committee Chair, Dr. Dail steadily guided and encouraged my curiosity and thought processes. Her tireless guidance during my academic tenure contributed significantly to my growth. Dr. Robin Dawson, Dr. Michael Wirth and Dr. Ashley Darcy-Mahoney provided expert qualitative, statistical, and neonatal scientific thinking which translated into a stronger research approach for this dissertation. Each committee member provided in depth reviews and clear direction into the research process and dissemination. I am honored to have been mentored by each of my committee members who have each have richly strengthened my scientific inquiry.

To the Robert Wood Johnson Foundation, thank you for choosing me as a Future Nursing Scholar.

And finally, to my UofSC PhD study cohort, thank you for the tears and smiles!

ABSTRACT

The advanced survival of the early premature infant (EPI) since the post-surfactant era has not improved many comorbidities. EPI comorbidities influence their lifelong health, social, and cognitive outcomes. EPIs often have immature and disorganized responses to stimuli during the neonatal period. EPIs respond to stressors from the Neonatal Intensive Care Unit's (NICU) environment, stimulation, or disease states based on physiologic system changes, often resulting in observable behavioral changes. Both physiologic and behavioral changes reflect autonomic nervous system (ANS) disruption, thus instability. Instability of the ANS due to chronic stressors, can lead to chronic physiologic dysregulation and lead to lifelong health comorbidities. Avoiding of instability in the ANS is crucial to prevent brain injury. Neonatal nurses are uniquely positioned to identify early indicators of behavioral and physiologic instability, allowing them to guide care that will prevent or reduce short and long-term comorbidities in the EPI. The best indicator of EPI instability is not yet known; therefore, the goal of this research was to identify indicators of EPI ANS instability, using physiologic and behavioral measures. Identification of early indicators of EPI instability can be utilized to optimize care plans for EPIs. This dissertation presents: the current state of the science; historical, conceptual, and theoretical frameworks; and, methodological approaches of research, which examine relationships between EPI instability and their behavioral and physiologic responses. A mixed methods, multiple subject within-case research study and

results are presented, in addition to a discussion regarding the development of further scientific evidence.

PREFACE

My desire to understand premature and ill newborns has been driven by my persistence and passion for delivering, guiding, promoting, and advocating for their best clinical care. My early mentors at the University of Maryland Neonatal Intensive Care Unit and my outstanding colleagues at the Greater Baltimore Medical Center have continually supported my pursuit to understand what more we can do to protect this vulnerable population. Since my early Neonatal Intensive Care experiences, I have learned and come to strongly believe that those we care for are telling us what they need, not with their own little voices, but by their actions. Just watch them, they will tell you what they need to develop: to be nurtured, comforted, and protected, within your caring hands.

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LIST OF ABBREVIATIONS

AA	African American
ABT	Abdominal Temperature
ANS	Autonomic Nervous System
BP	Blood Pressure
BT	Body Temperature
BW	Birthweight
CLD	Chronic Lung Disease
CON	College of Nursing
CPAP	Continuous Positive Airway Pressure
CPTd	Central-Peripheral Temperature Difference
CRIB	Central Risk Index for Babies
DOL	Day Of Life
ECG	Electrocardiogram
EMR	Electronic Medical Record
EPI	Early Premature Infant
EPIIM	Early Premature Infant Instability Model
FT	Foot Temperature
GA	Gestational Age
GE	General Electric
HIS	Hispanic

HPA..Hypothalamic-Pituitary-Adrenal

HR .... Heart Rate

HRV ....Heart Rate Variability

IRB .... Institutional Review Board

IVH ....Intraventricular Hemorrhage

MSB .... Minutes Since Birth

NEC... Necrotizing Enterocolitis

NICU..Neonatal Intensive Care Unit

NIDCAP...............Neonatal Individualized Developmental Care and Assessment Program

NPO... Nothing By Mouth

NSE .... Neonatal Stress Embedding

PCA..Post Conceptual Age

PNS ....Parasympathetic Nervous System

ROP..Retinopathy of Prematurity

RR ....Respiratory Rate

SNAP ....Score for Neonatal Acute Physiology

SNAPPE-II.................... Score for Neonatal Acute Physiology with Perinatal Extension-II

SNS .... Sympathetic Nervous System

SpO2 .... Peripheral Capillary Oxygen Saturation

SSC. .... Skin to Skin Care

U.S. .... United States

UofSC .... University of South Carolina

VLBW... Very Low Birthweight

CHAPTER 1

INTRODUCTION, BACKGROUND, AND CONCEPTUAL ANALYSIS

1.1 OVERVIEW OF CONTENT PROVIDED

Chapter 1 introduces and the significance of the problem. A concept analysis is presented to provide clarity and context for the identification of current knowledge related to stability and instability of the early premature infant (EPI). A brief overview of the autonomic nervous system (ANS), and physiologic and behavioral indicators of ANS instability is provided. Chapter 2 presents a literature review manuscript and identifies a gap in scientific evidence reflecting contemporary assessments of instability in the EPI. Chapter 3 presents a manuscript describing the theoretical framework to examine EPI instability. Chapter 4 presents a manuscript describing the methodological approach and feasibility testing of a coding scheme. This coding scheme was developed to discern between stability and instability/stress reactions using items adapted from the Neonatal Individualized Developmental Care and Assessment Program (NIDCAP), the scientific literature, and expert review. Additionally, results of a feasibility study using video observation to examine stability and instability periods in the EPI are presented. Chapter 5 presents the research which was conducted to determine if behavior or physiology, or a combination of both, is a better indicator of instability in EPIs before, during, and after nursing assessment. The qualitative and quantitative results are also presented. Finally, a conclusion and suggested areas for future research are recommended to further the continuum of scientific knowledge. Future prospective studies may lead to improved outcomes as a result of anticipatory clinical actions which identify and prevent EPI instability.

1.2 INTRODUCTION AND BACKGROUND

EPIs are defined as infants delivered before 34 completed weeks of gestation, and account for nearly 104,000 births (equating to 2.8% of live births) in the United States (U.S.) each year (Martin et al., 2019). EPIs who survive have a risk of developing disabilities which may impact lifelong social, cognitive, and economic outcomes (Cheong et al., 2018; Lee et al., 2020). EPIs have immature and disorganized responses to stimuli (e.g., asynchronous movements) while cared for in the Neonatal Intensive Care Unit (NICU) (Modrcin-McCarthy et al., 1997). The immature and disorganized response in EPIs from the environment, handling or stimulation, or disease states result in observable behavioral and physiologic changes, both of which reflect ANS disruption, thus instability (Als et al., 2004). Understanding the EPI behavioral and physiologic longitudinal responses based on ANS maturity is crucial to prevent short- and long-term comorbidities following birth (Als et al., 2004).

1.3 CONCEPTS OF STRESSORS AND INSTABILITY

According to the Merriam-Webster dictionary, the word instability is defined as the quality or state of being unstable (*Merriam-Webster*, 2020). Etymologically, instability is derived from the 15c Old French word “instabilite” meaning inconstancy, or from the Latin word “instabilitatem” meaning “unsteadiness” and “not firm, inconstant”, and from “in”, “opposite” of “stabilis” (*Instability (n.),* n.d.). (*www.etymonline.com*). Surrogate terms for instability include unstable, imbalance, and inconstancy.

The term physiologic is defined as relating to physiology, a characteristic of, or appropriate to, an organism's healthy or normal functioning or differing in, involving, or affecting physiologic factors (*Merriam-Webster*, 2020). Physiologic is derived from the 16c word physiological, defined as pertaining to a natural science (*www.etymonline.com*). For this research, the conceptual definition of physiologic instability is defined as the quality of the infant's behavioral state, motor, visceral or physiological response, which can be observed by physiologic and behavioral monitoring and noted as a variation from a normal state.

1.4 CONCEPT ANALYSIS

A classic concept analysis was conducted based on the Walker and Avant 2011 method of defining the abstract elements of the phenomena (Walker & Avant, 2005; Walker & Avant, 2011). Uses of the various and discordant terms related to the concept of physiologic instability across several disciplines, including Engineering, Pharmacology, Psychology, Medicine, and Nursing were identified. The concept of physiologic instability is critical to aid in understanding the potential to identify early predictors of change in status or early indicators of illness in the EPI.

To incorporate all uses of the concept of physiologic instability, a broad search was completed using dictionaries, thesauruses, and academic databases (Walker & Avant, 2011). A search of traditional neonatal textbooks was completed to identify historical references. Authoritative and premier databases of PubMed and Medline EBSCO were explicitly used to retrieve citations. Filters were applied to limit the search to publications of clinical trials in premature human infants and written in the English language. No limits were placed on publication dates while filtering the search. The results were screened by reviewing titles and abstracts to identify relevant scientific publications. Included articles were selected based on the population of interest and those referencing the term physiologic instability used to assess or determine changes in health status. Articles were excluded if they were not related to EPIs. Reference lists of the selected publications were reviewed for further source identification. MESH terms, “Infant, newborn” [MESH] AND “Instability” were used. Due to the substantial number of results, the search was further refined to “Infant, newborn” [MESH] AND “Instability AND “Preterm”. Further, “Physiologic instability” was added to the search term.

Following the literature search, 243 articles were identified. After reducing results by inclusion and exclusion criteria and removing duplicates, eighteen articles remained for full-text review, of which two articles were ultimately retained. Figure 1.1 shows the Prisma Flow Diagram (Shamseer et al., 2015) summarizing the results.

The concept of physiologic instability was used in several ways within the literature. For example, skin to skin care (SSC) has been demonstrated as an intervention to improve outcomes of premature infants and to stabilize cardiorespiratory adaptation (Bergman et al., 2004). SSC is controversial for infants receiving respiratory support in the NICU (Lorenz et al., 2017). Changes in the markers of physiologic instability were observed, including regional cerebral oxygenation, peripheral capillary oxygen saturation (SpO2), heart rate (HR), inspired oxygen, and skin temperatures. (Lorenz et al., 2017). Each marker was clearly defined to detect a variation from the predefined values before, during, and after SSC. The markers were identified as having a potential impact in oxygen supply to the brain, thus impacting outcomes (Lorenz et al., 2017).

A second example was related to detecting unexplained episodes of physiologic instability in preterm infants who are receiving respiratory support. It was also investigated to better understand some episodes of physiologic instability, which may impact neurodevelopmental outcomes (Marshall et al., 2019). Determining variation in SpO2 and HR following respiratory pauses were determined to be predictors of physiologic instability (Marshall et al., 2019). Predefined values were determined for each parameter, and variation from these typical values within sixty seconds of a pause was determined to be an indicator of physiologic instability. Predictors of instability were concluded to be gestational age (GA), hemoglobin level, type of respiratory support, medications, respiratory pause clusters, and duration (Marshall et al., 2019). Predictors of instability were all associated with respiratory support equipment.

The concept of physiologic instability, as identified in the literature, allowed the identification of shared attributes. The similar measurable parameters were SpO2 and HR. The dissimilar measurable parameters were cerebral regional SpO2, respiratory pauses, inspiratory oxygen, and axillary temperature. The period of observation also differed between studies (Bergman et al., 2004; Lorenz et al., 2017). A change in a variable from average, after 60 seconds following a respiratory pause, was considered unlikely to be related to instability (Marshall et al., 2019). Lorenz et al. stated there is an expected EPI physiologic instability following handling and transfer. The researchers incorporated a 30-minute washout period, when data was not collected, after the patient transfer before data was collected (Lorenz et al., 2017). The period without data collection attempted to ensure instability was related to handling and transfer.

Similar signs, symptoms, clusters, and characteristics of a the concept are used to derive and define the meaning of physiologic instability through attributes (Walker & Avant, 2011). The following attributes were identified from the literature review: the environment of care, including the microenvironment and macroenvironment of the NICU, and the immature or dysfunctional ANS. The microenvironment of the EPI's care during the NICU stay includes the incubator and patient support aides used for warmth and containment. The macroenvironment is the space in the NICU external to the incubator, and includes people, sound, noise, light, and activity. Concepts related to, and the opposite of physiologic instability are shown in Table 1.1.

Walker and Avant define antecedents as those events occurring before the concept's occurrence (Walker & Avant, 2005). To determinate physiologic instability, a caregiver must first recognize a change from the individual normal physiologic state. EPIs GA at birth and post conceptual age (PCA) reflect individual capabilities to indicate a variation from the expected normal state. Walker and Avant define consequence as an incident that occurs because of the concept (Walker & Avant, 2011). Comorbidities developed in the EPIs in the NICU include but are not limited to, hypothermia, hypoglycemia, cardiac and respiratory abnormalities, intraventricular hemorrhage (IVH), chronic lung disease (CLD), retinopathy of prematurity (ROP), infection, and necrotizing enterocolitis (NEC) (El-Atawl et al., 2018).

Empiric referents are measurable ways to demonstrate the occurrence of a concept (Walker & Avant, 2005). Physiologic instability reflects a variation in the EPIs normal state or vital signs. Measurable indicators of cardiovascular, respiratory, and thermal physiologic health changes results in a nursing response, a period of questioning or examination. Time reflects the period of observation used to detect a variation from normal state for an individual patient.

Clinicians use physiological monitoring and behavioral assessments to determine variation in patient status or instability (Als & McAnulty, 2011). Nurses continually care for the EPI through intermittent physical assessments and caregiving or procedures. Identification of changes in the EPIs vital signs and behavior are reported as physiologic instability of changes from a normal state. Individual parameter variation from expected norm includes those measurable indices of physiologic monitoring, HR, respiratory rate (RR), SpO2, and body temperature (BT), which are standard nursing vital sign measures in the NICU. Medical providers and advanced nurse practitioners may rely on nursing assessments and reports, objective trends in physiologic or laboratory measures based on electronic medical records (EMRs) and intermittent physical assessments. EPIs respond to stressors based on physiologic system changes resulting in observable behavioral changes, reflecting disruption in the ANS, thus instability (Als, 1986).

1.5 CONCEPTS OF STRESSORS AND INSTABILITY

"Stressors" and "instability" are concepts clinically used as an indicator of variation in EPI physiology and/or behavior. Clinicians and researchers do not use a standard definition for the concepts of stressor or instability. This research has defined a stressor as an action, activity, or environmental stimulant introduced to the infant, which lead to a sign or symptom of instability. This research also defines instability as a state, motor, or physiologic response that can be measured and noted as a variation from stability or normal state. Most often, a stressor may cause instability in the EPI. The concepts of stressors and instability which result in ANS variations are shown in Table 1.2.

EPI responses to stressors reflects immature and disorganized responses to stimuli (Modrcin-McCarthy et al., 1997). Chronic stressors lead to chronic physiologic dysregulation and lifelong health comorbidities due to impairment of the brain structure, body organs, metabolism, and normal physiology of biological systems (Shonkoff & Garner, 2012). Iatrogenic stressors in the NICU include caregiver handling (Lyngstad et al., 2014), touch, pain from procedures (Holsti et al., 2005), environmental light (Lebel et al., 2017), and noise (Aita et al., 2013). These interactions may result in physiologic and/or behavioral responses, leading to instability (Peng et al., 2009).

The clinical detection of infant stability is not universally defined and there is no standard definition utilized in the literature. Surrogate terms for stability include stableness, maturity, balance, constancy, and homeostasis. Generally, EPI stability is reflected by normal neonatal thermal and cardiorespiratory physiology during the transition to extrauterine life and subsequent NICU stay (Chi Luong et al., 2016). Normal physiological parameters vary across GAs and between individual infants based on gender, weight, and clinical context (Alonzo et al., 2018; Perez et al., 2019).

1.6 THE AUTONOMIC NERVOUS SYSTEM

The ANS contains two contrasting but complementary components which regulate and adjust BT, HR, respirations, digestion, motor system, and behavioral responses (Mulkey & du Plessis, 2019; Mulkey & Plessis, 2018; Reis et al., 2014). The ANS is comprised of the sympathetic nervous system (SNS) and the parasympathetic nervous system (PNS). Both the SNS and PNS regulate glands, smooth muscles, and cardiac muscles. The SNS responds to stressors as fight or flight reactions by increasing metabolic responses, while the PNS regulates, conserves, or balances metabolic consumption (Mulkey & Plessis, 2018).

During fetal development, there is a nonsynchronous maturation of SNS and PNS with the PNS acceleration maturation between 25-32 weeks GA (Mulkey & Plessis, 2018). The SNS is not completely developed at birth in either preterm or term infants, as demonstrated by studies of catecholamine levels (Lagercrantz & Marcus, 1992). The ANS is normally immature at term gestation and is primarily influenced by the SNS, which of importance to the EPI (Yiallourou et al., 2013).

Early fetal and neonatal exposure to stressors and the resulting instability can affect ANS maturation and function of the brain leading to comorbidities and mortality in the EPI (Mulkey & Plessis, 2018). Normally, the fetus has a catecholamine burst supporting cardiovascular, endocrine, and thermoregulatory responses at 30 weeks GA (Mulkey & Plessis, 2018). Infants born at full term gestation the release of catecholamines and hormones which support blood pressure, energy metabolism and thermogenesis during the fetal-to-newborn transition. These catecholamines may be decreased when an infant is born prematurely, thereby impacting ANS function (Mulkey & Plessis, 2018). ANS alterations due to immaturity and stressors result in cardiovascular, respiratory, and BT instability (Mulkey & Plessis, 2018; Patural et al., 2008).

ANS development, which occurs during the period of extrauterine growth and development during the third trimester, is crucial to prevent brain injury (Mulkey & Plessis, 2018). Preventing EPI brain injury depends on stability of ANS regulation of the cardiovascular system, cerebral autoregulation, and cerebral vasculature. SNS stress response alters HR and circulation to the brain and muscles via neurotransmitters and hormones. ANS dysfunction may be a contributor to or an early biomarker for EPI brain injury and poor neurodevelopmental outcomes (Mulkey & Plessis, 2018) and therefore, physiologic measurements of the ANS have been suggested to be a biomarker for long-term neurodevelopmental outcomes.

Physiologic indicators of PNS immaturity include central-peripheral temperature difference (CPTd) (Lyon, 1997, Knobel-Dail, 2017), heart rate variability (HRV) and blood pressure (BP) changes (Mulkey & Plessis, 2018; Shaffer & Ginsberg, 2017). CPTd gradients have been shown to differ based on vasomotor tone of the premature infant. Both HRV and BP change in response to sympathetic tone, which can be measured by the R-R interval. As the PNS function matures post-birth, differentiation of low frequency HRV and high frequency HRV is mediated by PNS and SNS respectively (Mulkey & Plessis, 2018; Shaffer & Ginsberg, 2017). HRV in the full term infant with hypoxic encephalopathy undergoing hypothermic treatment and rewarming has been found to be a physiologic biomarker of stress reactions (Metzler et al., 2017). HRV has also been used as an indicator of instability in the premature population (Aita et al., 2013; Cong et al., 2012; Cong et al., 2009).

1.7 PHYSIOLOGIC AND BEHAVIORAL INDICATORS OF AUTONOMIC NERVOUS SYSTEM VARIABILITY

1.7.1 PHYSIOLOGIC MEASURES

In clinical practice, measurements of wellness or instability are based on patient physiological monitoring, laboratory measures, intermittent physical assessment and patient responses to interventions and stressors. Physiologic stability or instability in the EPI can be observed by changes in HR, BT, RR, SpO2, skin color, tone, and activity and these changes represent variation in systems within the ANS.

Physiologic responses to stressors can result in increased blood perfusion to some areas of the body, decreased HR, and decreased gastric sections. The ANS regulates skin blood flow by vasoconstriction or vasodilation and sweating which affect BT (Tansey & Johnson, 2015). The EPI's ability to respond to cold stress via vasoconstriction is limited (Knobel et al., 2013) due to the immaturity of the ANS (Bini et al., 1980). Abnormal patterns in BT, represented by variation in thermal gradients as measured by CPTd, may represent signs of ANS dysregulation in response to stressors (Lyon et al., 1997). Measuring CPTd continuously reflects thermal differentials across the infant, therefore is a biomarker for perfusion patterns (Simbrunner, 1995). These abnormal temperature patterns are also associated with nursing care and activities. Recommendations for nursing management during procedures and handling following birth have been published (Bissinger & Annibale, 2010; Soll, 2008).

General nursing assessments in EPIs include routine monitoring of BT, HR, RR, BP, SpO2, and behavior. Methods of assessing physiologic indicators of stability versus instability and the frequency for which those measures are assessed vary based on patient demographics (such as, GA, gender, race, and birthweight (BW), patient illness, and nursing availability). BT is usually assessed intermittently using a digital or manual thermometer at the axilla, forehead, or ear, and rarely in the rectum (Ringer, 2013).

In addition, standard of care dictates continuous temperature measurement using a single or dual skin temperature probe when incubators or radiant warmers are used for patient care (Joseph et al., 2017). HR and RR are continuously monitored and measured with physiologic monitoring devices or intermittently via auscultation. BP can be measured intermittently by blood pressure cuff or continuously when intraarterial assess is in place. SpO2 can be continuously monitored by bedside pulse oximetry. Clinical assessment of skin color includes noting if the infant is jaundiced, pink, pale, webbed, red, dusky, or blue.

1.7.2 BEHAVIORAL MEASURES

In addition to physiologic indicators exhibited in EPIs, the ANS reacts with behavioral responses such as variations in tone and activity, digestive function, and elimination behaviors (Als, 1986). Behavioral responses to stressors in relationship to the digestive system in EPIs include emesis, burps, gags, and hiccoughs. ANS instability versus stability can be assessed through motor activity, which includes flexion, rotation, bringing the hand to mouth, sucking, and extension of the limbs. Motor responses to stressors include tremors, startles, twitches, and the movement of extremities and face. Researchers have assessed variations in ANS activity through sleep states, which include periods of rapid eye movement during light, awake, and active sleep states (Khalesi et al., 2017; Neu et al., 2000; Pressler, 2001).

Behavioral observations which aid in the evaluation of the SNS include assessment of the infant's ability to tolerate stimulation, such as routine care and procedures, parental handling, and environmental stressors such as noise and lights (Fleisher et al., 1995). As the EPI matures, improvement in the ability to tolerate interactions and stressors demonstrates stability and maturity. The Assessment of Premature Infant Behavior Model, which guided the development of NIDCAP assessments of premature infants, can be evaluated for stability and instability (Als et al., 2005; Brazelton, 1973). EPI responses to stressors are useful in maximizing neurobehavioral organization during caregiving in the NICU and promoting improved long and short-term outcomes (Als, 1999).

1.8 MEASUREMENT TOOLS AND ASSESSMENT

Several validated tools derived from medical or statistical methods based on ANS function are available for clinicians to aid in assessing infant stability, degree of illness, and assessment of behavior. These historically referenced tools, include the Apgar score (Apgar, 1953; et al., 1958), the Score for Neonatal Acute Physiology (SNAP) (Richardson et al., 1993), Score for Neonatal Acute Physiology with Perinatal Extension-II (SNAPPE-II) (Richardson et al., 2001) (the most recently updated), Central Risk Index for Babies (CRIB) (Ezz-Eldin et al., 2015; Lago et al., 1999), and NIDCAP (Als, 1986). It is important to note that these tools are tested and validated for specific time-periods in the trajectory of postnatal age, specifically from birth through discharge from the NICU.

The Apgar score (Apgar, 1953) reflects stability during transition from intrauterine to extrauterine life by using five physiologic indicators: HR, respiratory effort, reflex irritability, muscle tone, and skin color. Research has demonstrated the Apgar score, measured at 1, 5, and 10 minutes, can be predictor of long-term outcomes (Torday & Nielsen, 2017). Apgar scores in the premature infant reflect status at birth despite physiologic immaturity. Apgar scores are also associated with death and neurologic injury, such as cerebral palsy, epilepsy, and impaired cognitive function (Weinberger et al., 2000).

The SNAP tool (Richardson et al., 1993) and the subsequent revision, SNAPPE-II (Richardson et al., 2001), generate a prognostic score which reflects infant severity of illness between admission to the NICU and 12 hours of age. The SNAPPE-II has been validated in the EPI population to demonstrate severity of illness in the first 12 hours of life (Reid et al., 2015). Nine items (birthweight, mean blood pressure, lowest temperature, ratio of arterial oxygen partial pressure [PaO2 in mmHg] to fractional inspired oxygen (FiO2), lowest serum pH, urine output, seizures, Apgar score, and if small for GA) are given scores ranging from 0-5 points. The resulting total score reflects the condition of the infant and the interventions needed to maintain stability (Richardson et al., 1993). The SNAP and SNAPPE-II scores have been found to be predictors of mortality (Harsha & Archana, 2015).

The CRIB tool (Ezz-Eldin et al., 2015; Lago et al., 1999) uses seven items (birthweight, GA, presence of congenital malformations, base deficit in the first 12 hours of life, maximum percentage of oxygen delivery in the first 12 hours of life, gender, and admission temperature) to produce a score predicting mortality in very low birthweight (VLBW) infants, which are premature infants weighing less than 1,500 grams. The updated tool, CRIB II, eliminated variables, including admission temperature, that could impact the score (Dorling et al., 2005). Researchers have shown that the CRIB II score is associated with severity of illness in the first 12 hours of life for the EPI population (Ezz-Eldin et al., 2015).

Behavioral assessment, motor, and sleep states can be assessed through observing an infant’s behavior over the NICU stay using the NIDCAP assessment (Als, 1986). In addition, RR, HR, SpO2, physiologic responses, motor, digestive function, and elimination are assessments used within the NIDCAP assessment (Als, 1986). Objective and subjective physiologic and behavioral assessment of the infant's reactions to stressors are based on the infant's responses while cared for in the NICU. The assessment is based on maturity of autonomic, motor, and state subsystems (Als, 1986). The integration and maturation of these subsystems influences brain development. NIDCAP assessments are used to determine a threshold of stability based on the interaction and maturity of the subsystems formed from the Model of the Synactive Organization of Behavioral Development (Als, 1982).

Nurses and other healthcare personnel should base their decisions on when and how to interact with an EPI by using the synthesis of physiologic and behavioral signs of instability to minimize short- and long-term morbidity. Infants are most vulnerable in the neonatal period, or first 30 days of life (DOL); however, care of these vulnerable infants may continue for months as they grow and mature in the NICU. Repetitive chronic stress contributes to instability and interruptions in brain activity, leading to short- and long-term morbid outcomes (Weber & Harrison, 2019). Acute and chronic environmental stress exposures in the NICU include maternal separation, pain, light, sound, handling, procedures, infection, and cold environmental temperatures (Modrcin-McCarthy et al., 1997). The NICU care team's goal is to ensure early identification of reactions to stressors or conditions of instability. Early identification of stressors during clinical care promote adequate growth, maturation, and development of the EPI, which ultimately optimize health outcomes and support timely discharge. It is important that clinicians determine the best physiological and behavioral assessment tools for use. With multiple physiologic and behavioral assessment tools available, more research is needed to determine which combination of physiologic and behavioral variables will best predict which stressors leading to instability, therefore helping clinicians achieve optimal health outcomes in the EPI.

Based on the concept analysis and review of the literature, a conceptual definition of physiologic instability is the quality of the infants' behavioral state, motor, visceral or physiological response, which can be observed by physiologic and behavioral monitoring and noted as a variation from a normal state. Behavioral variables include the infants autonomic, motor, and state behaviors which indicate instability or stability based on the NIDCAP assessment (Als, 1986). HR, RR (Mulkey & Plessis, 2018), abdominal temperature (ABT), foot temperature (FT), and CPTd (Knobel-Dail et al., 2017; Mok et al., 1991) are physiologic variables used to measure instability. Stressors in the NICU environment and from care giving cause instability in the EPI (Aita et al., 2013; Taquino & Lockridge, 1999).

EPI chronic stressors, lead to chronic physiologic dysregulation and lead to lifelong health comorbidities due to impairment of the brain structure, body organs, metabolism, and normal physiology of biological systems (Shonkoff & Garner, 2012). Iatrogenic stressors in the NICU may include necessary handling and touch, pain from procedures, environmental light, sound, and noise. These stressors may result in physiologic and/or behavioral responses leading to instability (Weber & Harrison, 2019). The EPI responds to stressors based on physiologic system changes resulting in observable behavioral changes, reflecting disruption in the ANS, thus instability (Als & McAnulty, 2011).

Intervening to detect or allay instability directly impacts the structure and function of the EPI's developing brain (Als et al., 2004; Nist et al., 2019), which can permanently impact neurodevelopmental outcomes (Weber & Harrison, 2019). NICU nurses are uniquely positioned to identify early indicators of behavioral and physiologic instability, allowing them to deliver care that will prevent or reduce short- and long-term comorbidities in the EPI. To mitigate morbidity and improve short- and long-term outcomes in EPIs, research to find the optimum assessment measure to quickly identify physiologic instability is necessary (Nist, 2020).

The objective for this research is to determine if behavior or physiology, or a combination, is a better indicator of instability in EPIs before, during, and after nursing assessment. Based on EPI behaviors adapted from evidenced based NIDCAP (Als, 1982; Als et al., 2005; Brazelton, 1973), behavioral observations and longitudinal physiological data will be compared. By comparing behavioral indicators of instability reflecting stress from the traditional NIDCAP observation, longitudinal physiological indicators (HR, ABT, and CPTd) alone or a combination of both, to identify a better index for instability.

TABLE 1.1 RELATED AND OPPOSITE CONCEPTS OF PHYSIOLOGIC INSTABILITY

RELATED CONCEPT	OPPOSITE CONCEPT
Hemodynamic instability	Physiologic stability
Cardiorespiratory instability	Stable state and attention
Behavioral instability	Autonomic system stability
Developmental instability	Behavioral progression
Physiologic stress	Growth and developmental progression

TABLE 1.2 STRESSORS, INSTABILITY, AND AUTONOMIC NERVOUS SYSTEM VARIATION

STRESSORS	INSTABILITY	ANS Variation
Instigator	Response	Observation or Measurement
Touch/Handling	ANS, State, Motor	HR, SpO2, activity, digestive
Procedures/treatments	ANS, State, Motor	HR, SpO2, activity, digestive, pain
Noise	ANS, State, Motor	HR, SpO2, activity, digestive
Light	ANS, State, Motor	HR, SpO2, activity, digestive
Environment	Physiologic changes	CPTd, HR, SpO2, color, tone, activity, digestive

ANS: autonomic nervous system; HR: heart rate; SpO2: peripheral capillary oxygen saturation; CPTd: central peripheral temperature difference

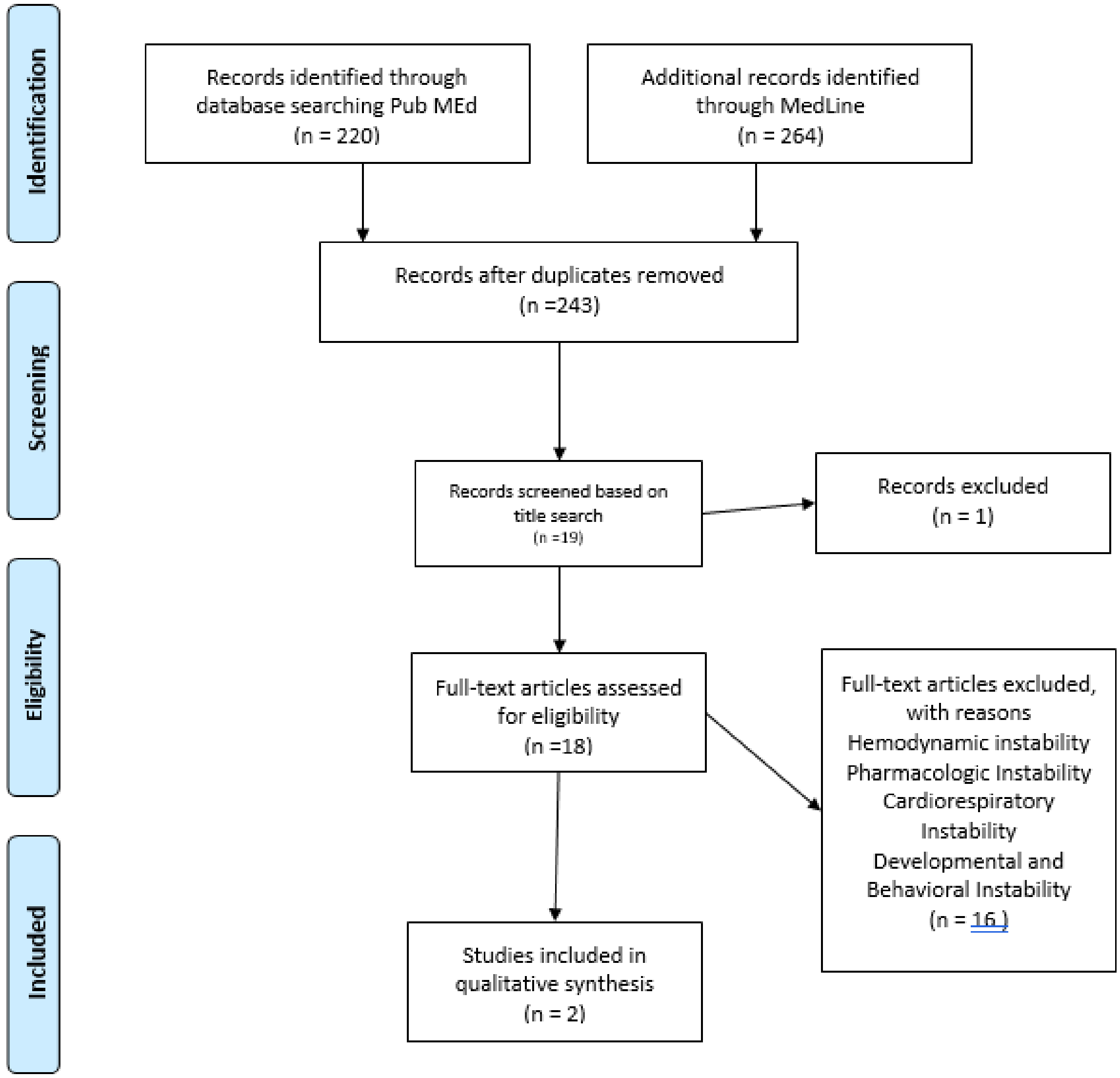

FIGURE 1.1 PRISMA FLOW DIAGRAM CONCEPT LITERATURE SEARCH

CHAPTER 2

EARLY PREMATURE INFANT STRESSORS AND INSTABILITY RESULTING IN AUTONOMIC NERVOUS SYSTEM DYSFUNCTION

2.1 ABSTRACT

2.1.1 PURPOSE

To purpose of this is to review the literature for physiologic and/or behavioral assessments for indicators of stability, responses to stressors, and risk for poor outcomes in EPIs.

2.1.2 METHODS

A search of PubMed and CINAHL databases was conducted to identify studies using physiologic and behavioral assessments to identify stability and instability in the EPI.

2.1.3 RESULTS

The search yielded 334 citations. 62 were assessed for inclusion, and 15 articles were ultimately selected for review and synthesis. The most frequently used measures were standard NICU vital signs including, intermittent or continuous HR, RR, and BT. None used longitudinal measures or CPTd to specifically assess autonomic stability. NIDCAP assessments was the most frequently used assessment tool to evaluate behavioral responses to stressors.

2.1.4 IMPLICATIONS FOR RESEARCH

Future studies should examine an assessment of infant stability using NIDCAP, longitudinal HR, BT, and CPTd for a more comprehensive assessment of ANS stability; this combination of tools may improve outcomes.

2.1.5 IMPLICATIONS FOR PRACTICE

NICU nurses who care for EPIs are uniquely positioned to identify early indicators of behavioral and physiologic instability. Identification of contemporary measures of instability may lead to improved short- and long-term outcomes for these vulnerable infants.

KEYWORDS

A. Preterm
B. Instability
C. Stressors
D. Neurodevelopmental Outcomes
E. Autonomic Nervous System

2.2 OBJECTIVE

The purpose of this literature review is to examine the current state of the science through reports of studies, which incorporate physiologic and/or behavioral assessments as an indicator of stability, responses to stressors, and risk for poor outcomes in the EPI. Literature was reviewed to identify which combination(s) of physiologic and behavioral assessments can be used to predict early reactions to stressors. Recognizing the best combination of assessments which identify stressors or instability, based on dysregulation of the ANS, will allow clinicians to mitigate stressors to the EPI and improve short- and long-term adverse outcomes in this vulnerable population.

2.3 METHODS

A broad search strategy was used in PubMed and CINAHL databases to identify published literature which described research related to assessments of stability versus instability, responses to stressors, and risks for poor outcomes in the EPI population. Specific keywords were used to select studies using assessment tools based on ANS physiologic and behavioral parameters including HR, HRV, BT, Apgar, NIDCAP, SNAP, and SNAPPE-II. Filters were applied to limit the search to publications of clinical trials in premature infants and to those written in the English language. Limits were not placed on publication dates. The results were screened by reviewing titles and abstracts to identify relevant scientific publications. Articles included were selected based on the population of interest and determinants of instability based on physiologic and behavioral variables commonly assessed to determine changes in health status. Articles were excluded if they were related to medical device comparisons for thermal management, brain cooling therapy, thermal dysfunction related to genetic disease processes, and sudden infant death syndrome, or if they were unrelated to EPIs or the topic of interest. Quality improvement or practice guideline implementations related to weaning from medical devices, devices investigated for thermal management without specific mention of stability, Kangaroo Mother Care, or SSC were also excluded. A secondary search by title eliminated duplicated publications. A search of traditional neonatal textbooks was completed to identify historical references. Reference lists of the selected publications were reviewed for further source identification.

MESH terms were used in PubMed to retrieve citations. These MESH terms included “Infant, newborn” [MESH] AND “Stability” OR “Stress” OR “APGAR” [MESH] OR “SNAPPE” [MESH] or “SNAPPE-II” [MESH] OR “NIDCAP” [MESH] OR “Temperature” [MESH] OR heart rate AND “Temperature” [MESH] OR heart rate variability. The CINAHL search terms included “Infant, newborn” AND “Stability” OR “Stress” “APGAR” OR “SNAPPE” or “SNAPPE-II” OR “NIDCAP” AND “Temperature” OR “Heart Rate” OR “Heart Rate variability”.

These searches yielded 334 non-duplicate references. After reviewing titles and abstracts, 286 articles were discarded because they were associated with the interventions to stabilize temperature, were review articles, were lacking analysis of parameters of interest, were related to outcome measures unrelated to the topic of interest, and/or were in a non-English language. One additional article was identified through reviewing a reference list of relevant articles. Articles about NIDCAP which related to outcomes measures after 18 months of age, parent perceptions, intrauterine growth restriction, feeding, Kangaroo Care, and pain were discarded. Articles retrieved for SNAPPE-II which were related to parent communications, delayed cord clamping, granulocytes, and infants greater than 36 weeks GA were discarded. Articles about Apgar which did not address physiologic or behavioral assessment of instability were removed. There were 42 articles assessed for inclusion by full-text review. Figure 2.1 shows the Prisma flow diagram (Shamseer et al., 2015) which summarizes the screening of articles reviewed, ultimately resulting in 21 articles.

2.4 RESULTS

There were 21 research articles related to reactions to stressors or instability in EPIs using physiologic or behavioral measures. Data from these 21 articles were organized under several matrix headings including year/author, study purpose, sample/study design, physiologic parameter or behavioral measurement and conclusions. Reports of studies described a mix of quantitative and qualitative methods. The sample sizes ranged from 30 to 3,268 infants or data sets. Broad categorization of the selected articles identified themes, which included behavioral assessment tools indicating stressors and physiologic indictors of instability.

2.5 BEHAVIORAL ASSESSMENT TOOLS

2.5.1 APGAR SCORE

Studies related to the use of the Apgar score were limited as most studies were conducted using mortality as the predicted outcome. The Apgar score demonstrates limited to moderate value of infant's stability or trajectory over the NICU stay. Researchers have recognized the limited ability of Apgar score to assess short- and long-term neonatal stability, which led to the need for further tools with a wider range of responses (Lee et al., 2010). Significant variation in assigning Apgar scores in premature infants have been described, which also limits its use across a wide GA range in premature infants (Rudiger et al., 2009). Additionally, the act of scoring an infant is subjective and there is not standard training to assure reliability. The Apgar score is not useful as a prognostic indicator of illness or mortality due to lack of reliability and the likelihood that each of the five components carries different clinical significance, despite having the same weight in scoring (Rudiger et al., 2009).

2.5.2 SNAP/SNAPPE-II

One prospective study of 141 infants was identified which evaluated usefulness of the SNAPPE-II tool after the first DOL to identify infants at risk for death or sepsis (Lim & Rozycki, 2008).The SNAP score was an indicator for length of stay, but not an indicator for sepsis or NEC. This study supported the original SNAP score intent as it was designed as an admission score and not intended for sequential scoring or to be calculated based on patient data from any time after admission (Lim & Rozycki, 2008). The SNAP and SNAPPE-II have been validated over birthweights to predict mortality from an assessment upon NICU admission. The score has not been validated to predict illness beyond admission in any GA over time.

2.5.3 NEONATAL INDIVIDUALIZED DEVELOPMENTAL CARE AND ASSESSMENT PROGRAM

Six articles were selected for their relevancy in addressing instability from associated stressors, specifically identified through NIDCAP assessments. NIDCAP behaviors are categorized into behavioral subsystems and indicate responses to stressors which can be used to assess instability and stability in the premature infant (Als, 1986). The NIDCAP assessment is the most evidenced based and validated tool used to date to assess underlying premature behavior. The NIDCAP assessment is supported by research in neuroscience, developmental and family psychology, medicine, and nursing (Westrup et al., 2000). Developmental interventions based on the NIDCAP assessment incorporate the holistic view of the infant and environment, which is reported to reduce stressful experiences in premature infants (Westrup et al., 2007). Individual reactions to stressors, associated with the ANS in EPIs, demonstrate the infants' abilities to respond and communicate instability to clinicians (Allinson et al., 2017; Alvarez-Garcia et al., 2014; Peters, 2001). Handling of the infant and associated interventions elicit significant changes in ANS responses and increased signs of instability. A well-regulated infant generally maintains stable temperature, color, HR, RR, SpO2, and tucked position and demonstrates good muscle tone. Organized infants will have unstable cardiac functioning changes noted in HR, labored breathing with desaturations, and changes in skin color (Sehgal & Stack, 2006). Improved stability with NIDCAP interventions has been shown to reduce CLD, growth, and length of stay, as well as improve developmental scores; NIDCAP interventions were postulated to be related to maturing ANS behavior (Als et al., 2004; Maguire et al., 2009; Peters et al., 2009; Westrup, 2007). In a further study, NIDCAP was demonstrated to greatly improve autonomic regulation in 107 infants less than 29 weeks GA (Zeiner et al., 2016). However, one study of 164 infants less than 32 weeks GA failed to demonstrate a difference between short-term growth and neurodevelopment at term equivalent age.

NIDCAP assessments have been shown to provide reliable and valid responses to stressors in EPIs (Wielenga et al., 2009; Zeiner et al., 2016). Compared to Apgar and SNAP/SNAPPE-II behavioral assessment tools, NIDCAP requires extensive training and demonstration of inter-rater reliability to complete the certification program. The NIDCAP assessment provides objective indicators of stability versus instability and is summarized to provide individualized patient care recommendations to caregivers and parents. These indicators describe interventions that can be used to promote continued neurobehavioral development while in the NICU. Limiting instable responses to stressors will decrease morbid neurodevelopmental outcomes.

2.5.4 PHYSIOLOGIC INDICATORS

2.5.4.1 BODY TEMPERATURE

Hypothermia is a known predictor of poor outcomes in newborns (Laptook et al., 2007). Premature infants with hypothermia on admission to NICU are known to have an increased risk of death and risk of infection. Using CPTd thermal gradients as measured by continuous central and peripheral temperatures using as an indicator of instability based on thermal gradients were mostly limited to caregiving and handling (Lyon et al., 1997). Researchers suggest using CPTd (Knobel-Dail et al., 2017) to predict autonomic instability associated with infection, as an inexpensive and quick predictive tool in the EPI. Historical assessment tools, such as Apgar, SNAP/SNAPPE-II, and NIDCAP, include HR measurements, but contemporary behavioral assessment tools do not include CPTd or HRV.

2.6 LIMITATIONS OF STUDIES

The studies selected for this review have limitations related to sample sizes and lack of consistency between methods and endpoints. There is a lack of consistency in terms used to indicate stressors, stability, or instability in the premature population. Studies reflect a wide variation in practice between the pre- and post-eras of surfactant treatment, as viability now includes a population of 22 weeks GA and beyond. Additionally, there is significant variability in the optimal timing for which these assessment tools can be used, with some being applicable immediately after birth, others within the first 12-24 hours, and still others applied across the NICU hospitalization. Because of all these variables, the studies selected were limited in relevance of their findings. A inherent limitation of literature reviews is the difficulty in reconciling conflicting findings between selected studies. Sample sizes varied and are often small, making findings non-generalizable.

2.7 DISCUSSION

The purpose of this literature review was to examine the current state of science of physiologic and behavioral indicators of instability in the EPI. The identification of an optimal combination of assessment variables can be used to predict and mitigate reactions to stressors, thereby decreasing the chance of morbid outcomes. Identified literature demonstrates the variability of ANS function across GAs in the EPI. This variation results in greater subjectivity and less specificity among assessment tools. It has been shown that stressors can lead to both physiologic and behavioral instability, thereby reflecting ANS instability. Physiological indicators of ANS instability are HR, HRV, and CPTd. Synthesis of 21 articles provide limited evidence of scientifically based early indicators of ANS instability in the EPI. Physiologic and behavioral assessment tools sparsely incorporate HR and single point BT measures; however, they do not incorporate HRV or identification of a unique combination of physiological and behavioral variables, reflecting ANS immaturity or dysfunction to use as a NICU clinical assessment tool to discern instability in the EPI is an area for future research. Development of an assessment to indicate EPI instability should provide a low cost, easily mastered, valid, and reliable clinical tool. From the review of literature, we hypothesize the use of stress and stability behaviors from the evidenced based NIDCAP assessments which already includes intermittent HR, RR, and SpO2, with the additional longitudinal HR, RR, SpO2 and CPTd measures, may provide the optimal assessment tool. This assessment tool could be developed to identify stressors, so that interventions can be applied to optimize stability and health in the premature infant.

2.8 IMPLICATION FOR PRACTICE

Based on the literature review, incorporation of longitudinal behavioral and physiologic measurements into neonatal nursing assessment as an indicator of stability or instability is not currently standard of care in the EPI. It is necessary for clinicians to consider perfusion and circulation patterns through surveillance of the longitudinal HR, RR, SpO2 and CPTd in observing EPIs during clinical assessments. The impact of longitudinal physiologic parameters may be an under recognized, which clinicians should incorporate in behavioral assessments as infants progress through their NICU stay. Ensuring decisions incorporate indicators of early instability or stressors to guide a successful transition towards discharge may lead to optimizing neurodevelopmental outcomes and potentially decreasing length of stay.

2.9 LIMITATIONS OF THIS LITERATURE REVIEW

The limitation of this literature review is that two databases were used and were limited to English language. There is a lack of a standard keywords to indicate EPI instability related specifically to physiologic parameters. In addition, the exclusion criteria may have limited identification of further studies which could add additional relevance to this topic.

2.10 CONCLUSION

The goal of this literature review was to identify common assessments used by clinicians to detect stability and instability in EPIs. Practical caregiver assessment would include the integration of longitudinal behavioral and physiologic measures. Behavioral measures would include infant autonomic, motor, and state behaviors. Physiologic measures would include routine vital signs currently obtained by including ABT and incorporating contemporary measures such as CPTd. Further research is needed to examine using NIDCAP evidenced based behaviors and CPTd as the optimal tool to predict instability and facilitate optimizing care to decrease morbidity and mortality in the EPI.

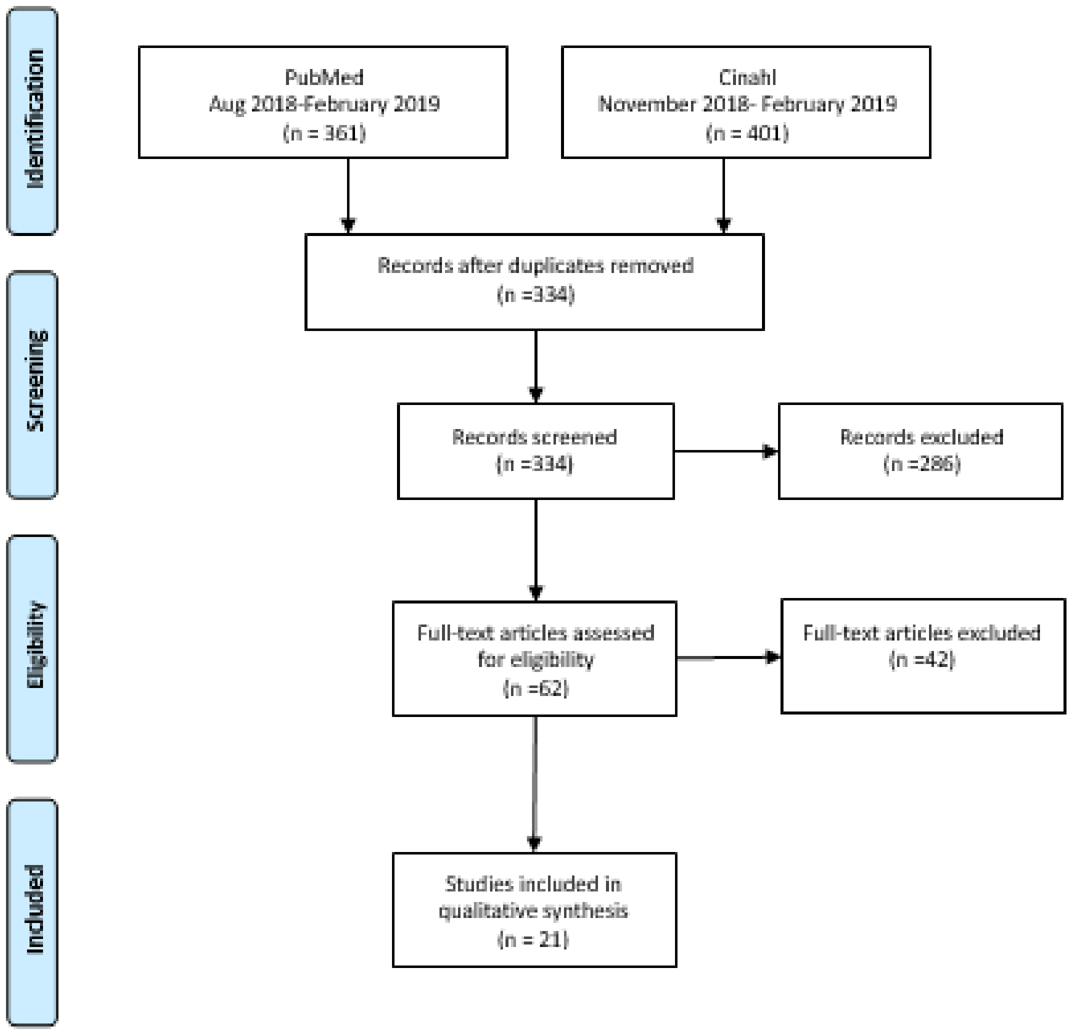

FIGURE 2.1 PRISMA FLOW DIAGRAM STATE OF THE SCIENCE LITERATURE SEARCH

CHAPTER 3

EARLY PREAMATURE INFANT PHYSIOLOGIC AND BEHAVIORAL INDICATORS OF AUTONOMIC NERVOUS SYSTEM INSTABILITY: A THEORETICAL MODEL

3.1 ABSTRACT

Few theoretical nursing models have guided nursing research to examine ANS instability in the EPI. Identification of modifiable indicators of ANS instability can be differentiated with changes in HR, RR, SpO2, and CPTd. A new theoretical model to identify physiologic and/or behavioral indicators of instability in EPIs may lead to an improvement in neurodevelopmental outcomes. This new theoretical model will help nurse researchers examine physiologic and/or behavioral indicators of instability in EPIs and may lead to improved neurodevelopmental outcomes.

KEY WORDS

A. Early Premature Infant

B. Nursing

C. Neonatal Intensive Care

D. Physiologic Instability

E. Neurodevelopmental Care

F. Autonomic Nervous System

3.2 INTRODUCTION

Limited theoretical models have guided nursing research addressing behavioral and physiologic instability of the EPI. EPIs are defined as infants born before 34 completed weeks GA. ANS variation, or changes in homeostasis, and the resulting impact on health outcomes have been examined in toddlers and children (Alkon et al., 2011; Bush et al., 2017; Stephens et al., 2020); however, nursing theoretical models that examine ANS changes in the EPI population are limited.

Instability is defined as the quality or state of being unstable (*Merriam-Webster*, 2020). Instability can be defined conceptually as a behavioral state, motor, visceral, or physiological response (Horowitz et al., 1978; Mok et al., 1991). Physiological instability can be measured with physiologic monitoring and is noted as a variation or change from the normal state of an individual. HR, RR, SpO2, and BT are standard physiologic variables used in the NICU. Behavioral instability can be observed as a variation or change from a normal state of an individual. Both physiologic and behavioral instability can be a response to stressors (Catelin et al., 2005; Choudhary et al., 2016). Stressors in the NICU environment, such as staff, equipment noise, sound levels, and care giving, including touch, handling, and positioning, cause instability in the EPI (Aita et al., 2013; Peng et al., 2009; Taquino & Lockridge, 1999).

A new theoretical model will help researchers examine physiologic and/or behavioral indicators of instability in EPIs and may lead to improved neurodevelopmental outcomes. The introduction of the Early Premature Infant Instability Model (EPIIM) presents relationships between physiological and behavioral variables, based on the ANS, to guide researchers to identify new predictive indices for EPI instability which can result in short- and long-term positive neurodevelopmental outcomes.

3.3 OBJECTIVE

The objective of this paper is to describe two existing theoretical models related to instability and stress in the EPI. A new theoretical model will be introduced which can be applied to future research methods to examine variations in ANS and EPI instability.

3.4 BACKGROUND

EPIs are defined as infants delivered before 34 completed weeks of gestation, and account for nearly 104,000 births (equating to 2.8% of live births) in the U.S. each year (Martin et al., 2019). EPIs are at risk of developing comorbidities due to their premature and underdeveloped ANS (Mulkey & Plessis, 2018; Patural et al., 2008). EPIs may develop comorbidities such as brain injury, chronic lung disease, visual problems, cardiac and metabolic disruptions, and infection while in the NICU (El-Atawl et al., 2018). These comorbidities can continue to affect lifelong social, cognitive, and economic outcomes, ultimately costing 26 billion U.S. dollars annually in health care spending (Cheong et al., 2018; *Preterm birth: causes, consequences, and prevention.*, 2007).

Nurses at the bedside need early indicators of instability in the EPI to deliver care that will prevent or reduce short- and long-term comorbidities. The immature ANS results in absent, dampened, or hyperreactive responses to stressors, the extrauterine environment, and necessary handling to provide care (Weber & Harrison, 2019). Clinicians and researchers use physiological monitoring and behavioral assessments to determine instability, which is detected by changes in patient status (Als & McAnulty, 2011). These assessments evaluate the maturity of the behavioral responses and changes in physiologic parameters which reflect the autonomic, motor, state, attentional, and self-regulatory subsystems in the EPI (Als et al., 2005). Changes in the subsystems may be indicative of EPI instability.

Environmental stressors in the NICU, such as sound, noise, lighting, and care giving and handling may cause instability in the EPI (Aita et al., 2013). HR, RR (Mulkey & Plessis, 2018), ABT, FT, and CPTd (Knobel-Dail et al., 2017; Mok et al., 1991) are variables used to measure instability. By incorporating these relatively new indices of EPI instability, such as ABT and CPTd gradients, within theoretical nursing models, EPI assessments may lead to improved outcomes.

3.5 THEORETICAL MODELS

Currently, two existing theoretical models provide frameworks for research related to EPI instability. The primary historical theoretical model is the Synactive Organization of Behavioral Development Model (Als, 1986). This psychology-based model is shown in Figure 3.1. This model describes the interaction between fetal/newborn development, based on GA, and the intrauterine and extrauterine environment. These interactions impact neurodevelopmental outcomes (Als et al., 2004).

In this model, premature infant behavioral and physiologic responses (Als et al., 1986) reflect the maturity of the developing autonomic, motor, state, attentional, and self-regulatory subsystems. Each subsystem works together and influences one another. Behavioral responses include changes in the infant’s expressions, activity, respiratory, or sleep states (Als et al., 1986). Physiologic responses include changes in color, HR, RR, or SpO2 (Khalesi et al., 2017; Lebel et al., 2014). Subsystem interactions reflect the interaction between the environment and the fetal/newborn maturity and physiologic functioning, motor activity, and state organization. Caregiver actions following birth, including developmental care practices, parent and staff behaviors, and necessary procedures, affect the newborn's developing ANS' ability to maintain equilibrium (Lester et al., 2011).

The combination of the NICU's environmental stressors, GA, and the developing ANS subsystems are interrelated and affect each other (Mackinnon, 2011). The NICU environment provides the most frequent stressor to the EPI. The environment is the NICU setting, including equipment, staff, families, sound, light, and caregiving interactions. Continuous exposure to environmental stressors of immature subsystems results in behaviors of disorganization and signs of stress (Alvarez-Garcia et al., 2014). Clinicians should be able to use evidence-based practices to minimize instability by basing actions on the behavioral and physiologic observations indicating an EPI's ANS response to stressors within the NICU (Altimier & Phillips, 2013; McAnulty et al., 2010).

Developmentally supportive care for premature infants has been operationalized in the NIDCAP (Als & McAnulty, 2011). NIDCAP assessments, analyses, and recommendations are based on four assumptions of the Synactive Organization of Behavioral Development Model (Als et al., 2005). The first assumption is that observations of an infant's behavior provide a scientific basis for designing interventions to minimize instability or stress responses and optimize the infant's development. Importantly, the second assumption maintains that the patients' families are to provide optimal co-regulatory support within this program. The third assumption is that NICU staff will be guided through this theoretical education in their care practices while performing stressful procedures such as suctioning, positioning, and invasive procedures, including those that result in pain. Finally, the fourth assumption is that new methods of environmental and physical care for the premature infant will lead to improved neurobehavioral outcomes, parent well-being and functioning, and professional and personal development in staff (Altimier & Phillips, 2013; McAnulty et al., 2010).

The second theoretical model currently used within the premature infant population around neonatal stress and neurodevelopmental outcomes is the Neonatal Stress Embedding (NSE) model (Nist, 2017; Nist et al., 2019). The NSE model describes the relationship between exposure to stressors in the neonatal period and neurodevelopmental outcomes in the premature infant. This model is based on biological embedding of the childhood adversity model stemming from the life course theory (Nist, 2017). Exposure to early life stressors, such as intensive care handling and care giving practices, as well as exposure to the environment, creates a memory pathway for the developing premature brain, which impacts the immune system, ANS, hypothalamic-pituitary-adrenal (HPA), and gene expression (Nist et al., 2019). Core concepts of stress, neuroscience, molecular immunology, epigenetics, and developmental physiology are critical developmental and maturational periods, which, according to this model, increases the susceptibility to premature brain injury.

In this model, prenatal environment and maternal attributes or interactions will cause variation in responses to stressors. Examples of acute and chronic environmental stressors in the NICU include maternal separation, pain, light, sound, handling, procedures, infection, and cold stress (Aita et al., 2013; Allinson et al., 2017; Als & McAnulty, 2011; A. J. Lyon et al., 1997). Prenatal stress exposures due to maternal exposure to stressful life events, illness, or substance abuse, and postnatal exposure to stressors in the NICU environment can cause variation in stress responses. The NSE model links the identification of potential stressors which may cause variable stress responses and the idea that repetitive stress exposure will cause memorization of or embedding of the stress exposure into the brain structure during the neonatal period. The alteration in brain structure and function because of the repeated stress exposure leads to negative neurodevelopmental outcomes (Anand & Scalzo, 2000; Nist et al., 2019).

In the NSE model (Nist et al., 2019), ANS functioning, gene expression, immune functioning, and HPA axis functioning, will shape the resulting brain structure/function and neurodevelopmental outcomes. The SNS responds to stress with changes in HR and HRV (McCain et al., 2005). Limited studies are available to show long-term effects of stress on the HPA axis and gene expression; however, early research has been completed in animals (Lupien et al., 2009). For example, increased cortisol levels associated with increased stress may be related to changes in gene expression generated by the HPA which is linked to neurodevelopmental impacts (Sullivan et al., 2017). Research also has initially demonstrated differences in outcomes between premature and full-term infants related to HPA function and behavior. The assumptions of the biological embedding of neonatal stress model support the theories underlying the principle of early life stress exposure on neurodevelopmental outcomes beyond that predicted by other disease complexities and multifactorial causes (Nist, 2017; Nist, 2020).

The framework presented in the Synactive Organization of Behavioral Development Model describes observational methods to record newborn behavioral responses to stimuli based on maturity and state of consciousness, thereby corresponding to behavioral disorganization and stress (Als & McAnulty, 2011). The NSE model includes ANS physiologic changes which are measurable attributes that indicate stress and instability (Mulkey & Plessis, 2018; Reis et al., 2014). Researchers can use the NSE model to empirically identify early indicators of instability, resulting in alteration of the brain structure and function.

The application of the two previous theoretical models facilitates structured and systematic examination of ANS instability. These models aim to describe, predict, and explain EPI instability; however, there are gaps in the models. Both models fail to consider the longitudinal picture of physiological data, such as HR, RR, BT, and CPTd or thermal gradient. CPTd is a good indicator of perfusion instability that goes along with illness and stress, it should be incorporated into any model based on ANS. The Synactive Organization of Behavioral Development Model has been widely used in the NIDCAP research (Als, 1999; Als & McAnulty, 2011; Fleisher et al., 1995; Holsti et al., 2004; McAnulty et al., 2010; Westrup et al., 2000). There has been limited application of the newer NSE Model (Nist, 2020) in current research.

3.6 THEORETICAL FRAMEWORK: EARLY PREMATURE INFANT INSTABILITY MODEL

Changes in HR, RR, SpO_2, and BT alterations (Knobel-Dail et al., 2017; Knobel et al., 2010; Leante-Castellanos et al., 2017; Mok et al., 1991; Stone et al., 2013) represent indicators of ANS instability and are easily measured and displayed. Currently, monitoring central and peripheral temperatures and their associated variations are not standard care, but they can be a good indicator of thermal instability and thermal gradients across an infant's body, which indicates perfusion stability. Combining key components of the Synactive Organization of Behavioral Development model and the

NSE model with longitudinal measures of infant stability, including BT, may lead to the identification of new predictive indicators of ANS instability in the EPI.

A new theoretical model based on physiologic indicators of ANS instability which includes HR, RR, and BT, with additional concepts from the two historical models, may be more predictive of EPI instability. Using constructs from historical theories of early life stress and stress exposure affecting premature brain development, (Als et al., 1986; Nist et al., 2019) our team developed the EPIIM (see Figure 3.2). The EPIIM represents specific inclusion of measurable mediators, including HR, RR, and thermal gradients which can be determined by CPTd. The CPTd measure has been shown to indicate instability when thermal gradients are either abnormally large (>2°C) or abnormally small differences (<0°C) (A J Lyon et al., 1997). These abnormal thermal gradients being indicative of ANS alterations seen with instability (Knobel-Dail et al., 2017; Knobel et al., 2009). The development of a new theoretical model will help provide future direction for what is known and unknown. This model can provide a foundation to generate further knowledge in determining better indices of EPI instability.

The constructs of the theoretical model include environment, health conditions, and health experiences of the EPI. Sound, noise, and light are NICU environmental constructs. Health conditions are those illnesses of prematurity including respiratory, cardiac, gastrointestinal, immunologic, and neurological illnesses. Health experiences reflect caregiver interactions, including touch, handling, positioning, comfort, and protection. The constructs link to the concepts of EPI stress experience, physiologic state capabilities and ANS alterations. Each of the constructs may empirically contribute to EPI illness modified by the GA and postnatal age resulting in physiologic changes.

Interactions between the concepts and empirical level processes contribute to indicators of EPI instability.

Measurements which can explain conceptual relationships include behavioral observations and physiologic assessments. After birth, there is a temporal relationship between environmental stimuli and brain development (Shonkoff et al., 2012). Behavioral maturation is reflective of the maturity, stability, or instability of the newborn primarily as seen through interaction between newborn and the caregiver. Ill-timed stimuli are disturbing to the infant, the ANS, and subsystem function (Als et al., 2004) particularly in the EPI when cared for in the intensive care environment of the NICU.

Premature infants have demonstrated the capability to display behaviors that can be associated with stimuli and activity (Liaw et al., 2012; Peng et al., 2009; Williamson & McGrath, 2019). Within the autonomic subsystem, changes in measurable HR and RR and observation of skin color changes can be recorded in conjunction with subsequent subsystem changes in movement and state (Holsti et al., 2004). Observations of behavioral activity within the subsystems have been associated with stress or adaptive responses which reflect stability or instability (Als et al., 1986). Specific ANS measures include measures of HR, RR, SpO_2 and BT. Changes in status or signs of illness can be reflected in the physiologic state capabilities of the EPI.

The EPIIM retains the consistent behavioral observations of the autonomic, motor, state, attentional, and self-regulatory subsystems from Synactive Organization of Behavioral Development Model (Als et al., 1986). The Model retains environmental influences which may have differing effects on the EPI responses to stressors when introduced at varying postnatal GAs. The EPIIM depicts the interactions among and between the concepts which have an impact on the EPI's ANS and methods of assessment for indicators of ANS instability.

Our new EPIIM has several assumptions. The extrauterine environment of the NICU and the associated necessary handling of an infant due to care is stressful to the developing EPI. The way the EPI responds to the environmental and stimulation stressors varies by their GA at birth and postnatal age at the time of the interaction. This response may impact brain development and associated neuro-outcomes. These responses can be measured and observed using autonomic, motor, state, attentional, and self-regulatory subsystem behavioral and physiologic indicators and will detect instability. The final assumption is that astute caregivers may detect signs of instability earlier in the premature infant as reflected by physiologic changes of HR, RR, SpO_2, and/or BT. Adding physiological indicators of ANS responses to stressors should add more information to the existing theoretical models and provide a more conclusive assessment of instability in the EPI.

3.7 SUMMARY/CONCLUSION

Two historical models related to the phenomena of EPI instability that may affect neurodevelopmental outcomes were presented. Based on a review of the historical models, an adapted model, the EPIIM, was developed and introduced. The new predictive EPIIM and the associated concepts were presented as one way to understand the interactions between stressors and the environment for the EPI in terms of ANS responses. ANS responses may vary by gestational and postnatal age which indicate instability. A set of constructs, concepts, definitions, and propositions explains the model by illustrating the relationships between the variables. Researchers may apply this new model to future research to identify the relationship between instability and EPI neurodevelopmental outcomes.

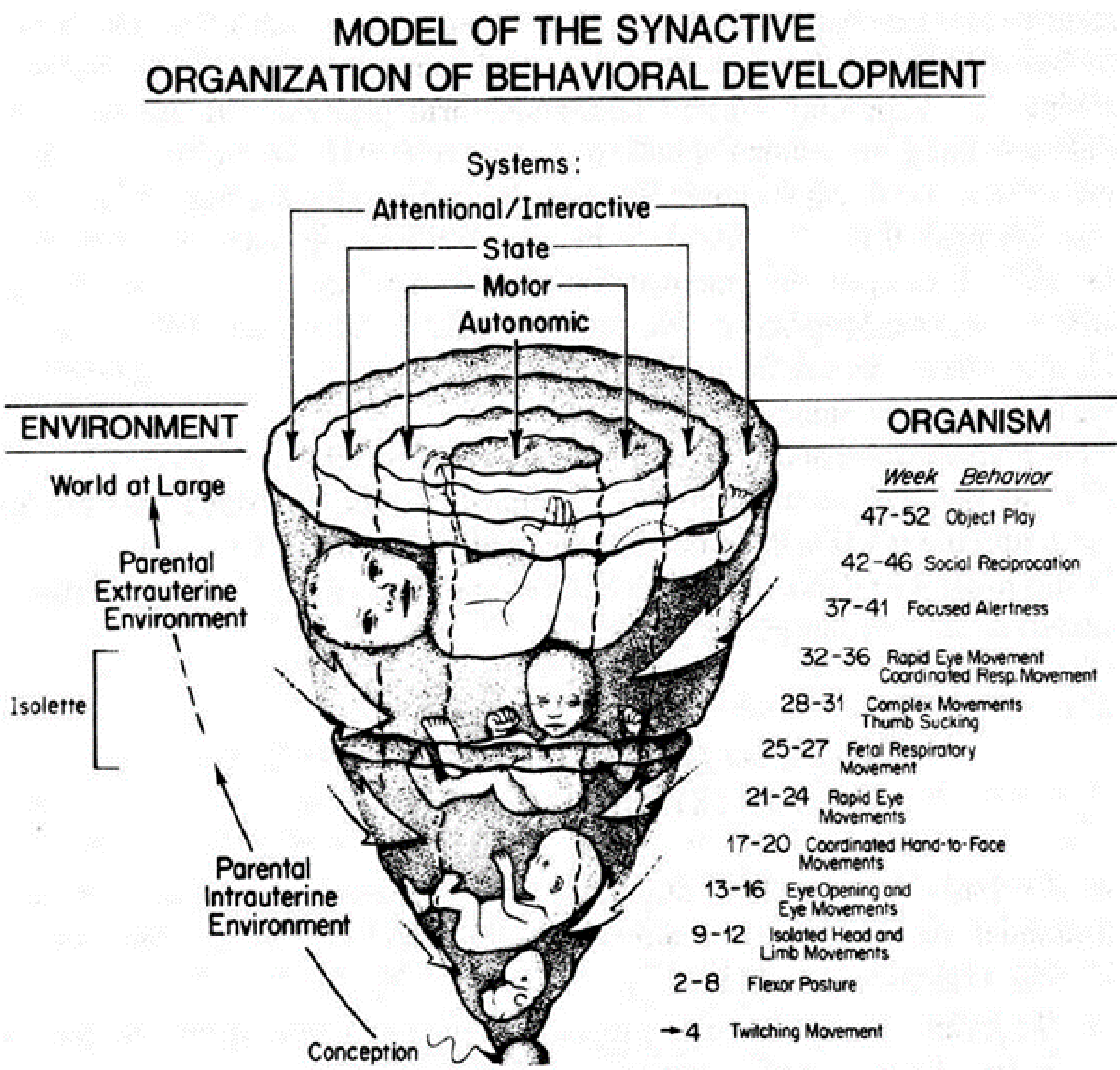

FIGURE 3.1 MODEL OF THE SYNACTIVE ORGANIZATION OF BEHAVIORAL DEVELOPMENT (ALS, 1986)

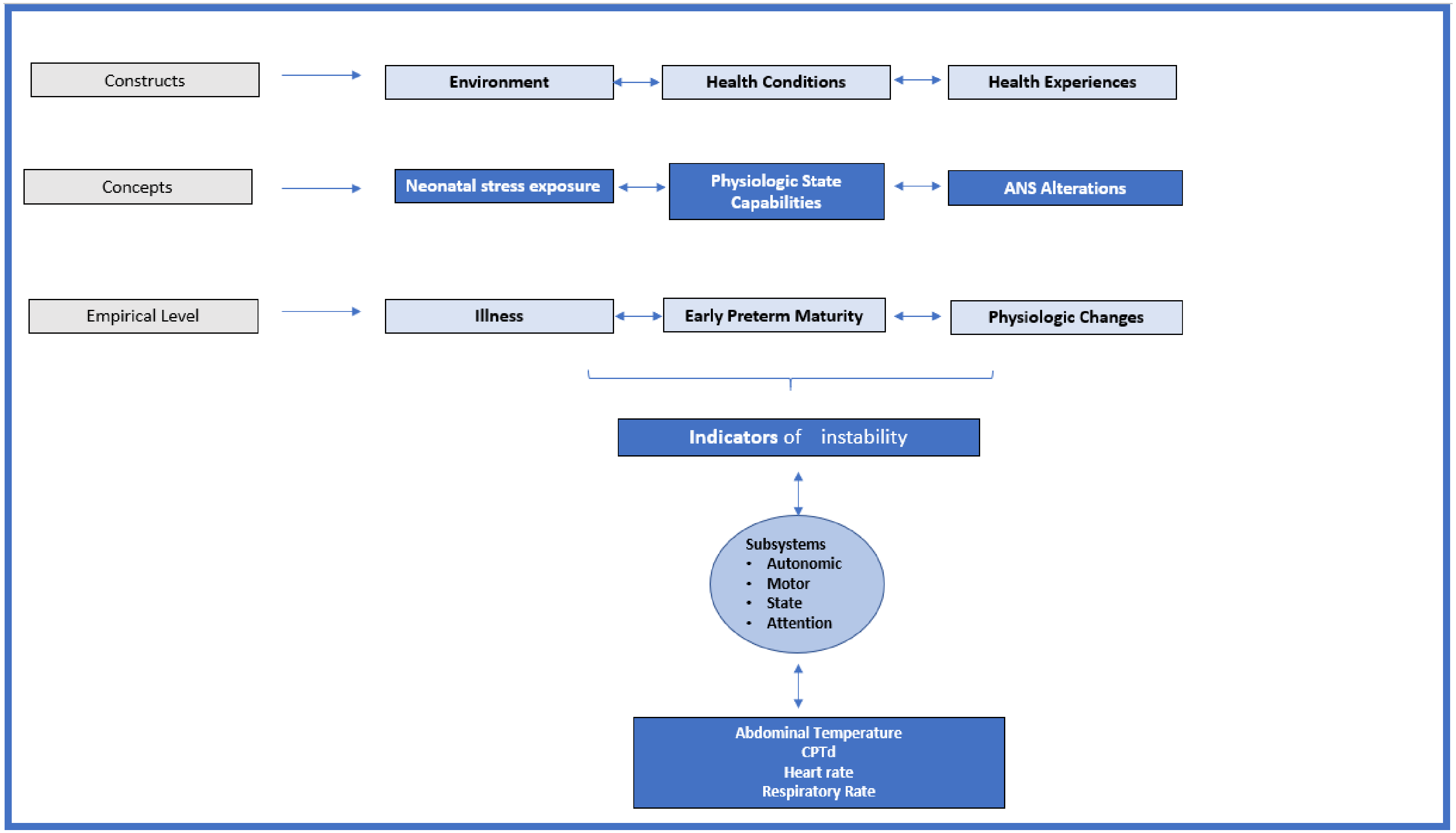

FIGURE 3.2 EARLY PREMATURE INFANT INSTABILITY MODEL

CHAPTER 4

OBSERVATIONAL METHODS TO EVALUATE STABILITY AND STRESS RESPONSES TO NURSING CARE IN THE EARLY PREMATURE INFANT USING NOLDUS OBSERVER XT.14® SOFTWARE

4.1 INTRODUCTION

The purpose of the paper is to describe research methods using video observation to examine stability and instability periods in the EPI. EPI's physiologic changes and behavioral responses to the environment and caregiving can reflect ANS disruptions and changes in health status, which lead to overall health system instability. The current standard of care relies on detection of instability based on episodic clinical assessment, astuteness, and continuous physiologic monitoring and it lacks a comprehensive longitudinal bedside evaluation. A coding scheme was developed to discern between stability and instability/stress reactions, using items adapted from the NIDCAP observation sheet, scientific literature, and expert review. The coding scheme was then used to code secondary data from a previous study. The data included six caregiving events in the same infant, consisting of 336 minutes of video recording before, during, and after nursing caregiving interactions in a NICU, within the infant's first 27 hours of life. Noldus Observer XT.14® software was used to facilitate data analysis, resulting in the identification of 1,798 combined stable and unstable coded behaviors. The coding scheme used in this feasibility study demonstrates the efficacy of coding EPI reactions to nursing care as stable or instable/stress responses. This method can be used to synthesize qualitative behavioral data and longitudinal physiologic data to determine the best assessment model for early detection of ANS instability.

Mixed method longitudinal studies among the EPI population aimed at understanding infants' responses to stressors have scarcely been conducted in the literature. In neonatal research, coding schemes have not been used to examine indicators of instability, instead they have focused on pain and stress reactions (Bellieni et al., 2007; Grunau et al., 2006). Using a behavioral coding scheme to code EPIs' reactions to caregiving during video observation may strengthen qualitative data collection methods. Therefore, the purpose of this paper is to describe an observational coding scheme and feasibility study with one infant to assess stable and instable behavioral responses based on the evidenced based premature infant behaviors of the NIDCAP assessment. This method will then be incorporated in a pilot study to examine longitudinal physiological data in comparison to behavioral assessment to detect instability in EPIs.

4.2 METHODS

Data for this feasibility study was collected, with the end goal of piloting a new methodology to study EPIs' stress and stable behaviors, during six assessments of one infant. Secondary data was obtained from a previous study (NIH/NINR: 1R15NR012157-01) which took place at a NICU in the southeast U.S. from 2010-2013 (Knobel-Dail et al., 2017; Knobel et al., 2013). This NICU is a Level III nursery within a Children's Hospital and Regional Training NIDCAP center, making it an ideal setting to examine the phenomenon of EPI instability. The parent study included infants less than 29 weeks

GA and less than 1,200 grams at birth. A bedside videorecorder was used to film each infants’ first five DOL. Video data were stored as Mpeg files, consisting of approximately 8-12 hours of video data per file, with approximately 8-10 video files stored for each infant. A copy of these data was transferred from the institution with an Institutional Review Board (IRB) agreement between the principal investigator’s previous institution and her new institution. IRB approval was obtained at the University of South Carolina (UofSC) to use these data for this feasibility methods study.

4.3 DEVELOPING THE CODING SCHEME

The coding scheme was developed to explicitly define behaviors known to indicate stability or instability (stress) in EPIs based on evidenced based models (Als et al, 1986). As shown in Figure 4.1, the primary steps in the coding scheme were: (1) identify EPIs’ behaviors which represent stability or instability; (2) clearly define each behavior; (3) apply the code within a software management tool; and (4) conduct analysis, refinement, and feasibility testing.

To answer the research question and ensure the coding scheme was valid and theoretically based, the developed scheme was adapted from the NIDCAP observation document (H. Als, 1986), scientific literature (Peters, 2001), and reviewed by doctorly-prepared neonatal experts (i.e., Neonatal Nurse Practitioner and Neonatal Physical Therapist) trained in premature infant behavior and neonatal research. This coding scheme aimed to achieve simplicity by maintaining similar levels of descriptions for each behavioral response, precise boundaries for behavioral distinction, and avoidance of a combination of codes (Bakeman & Gottman, 1997). The coding scheme defined 110 physical-based behavioral codes embodying distinctions for assignment of infant behaviors (Bakeman & Gottman, 1997). The behaviors were based on the evidenced based newborns' autonomic, motor, and state behavioral subsystems, as described in the Model of the Synactive Organization of Behavioral Development (Als, 1982; Als et al., 1986).

The autonomic subsystem includes RR, skin color, neurologic status, and visceral status (Als, 1986). The motor subsystem includes gross motor, facial, and extremity movements (Als, 1986). The state subsystem includes the level consciousness (sleep state) and attention-related behaviors (Als, 1986). These behaviors are reliable and valid among prematurely born infants who are cared for in the NICU (Als & McAnulty, 2011; Holsti et al., 2004; Maguire et al., 2009; Pressler, 2001) (see Table 1, subsystem behaviors reflecting stability or instability).

Coding observations of stability or instability followed the codebook definitions of behaviors developed for behavioral observation. Indicators of stress are represented by understanding the combination of autonomic, motor, and state subsystem stress behaviors associated with the clinical context, rather than single isolated behaviors (Als et al., 2005).

Each behavioral code was identified as a state or point behavior (Grieco et al., 2017). The codes within each subsystem are mutually exclusive and exhaustive, allowing frequency counting of identified behaviors (Martin & Bateson, 2018) to associate with the clinical context. A state event is an event with a distinct start and end such as deep sleep state. Analysis of state events can focus on the state event's duration, and with analyzing duration of sleep states, interventions, or time of hand containment. If the analysis does not require duration, then point events can be evaluated to determine the behavior rate. Point events, such as startles, finger splays, or bracing leg activities, are unrelated to duration of time, are momentary, or have zero duration. The combination of point and state events and the clinical context provides a qualitative description of behaviors for further analysis.

The coding scheme was tested in this feasibility study using the preliminary definitions to provide opportunities to clarify and define clear boundaries that describe behaviors. Based on the ability to visualize the infant in the video frame, it was determined that the descriptions for some behaviors needed further explicit clarification. The coding scheme was revised to clarify sleep states and further define state and point events. Subsequent behavioral observations were completed with the revised scheme to assess infant videos. Further feasibility testing was then completed on the remaining four videos.

4.4 METHOD FOR DETERMINING OBSERVATION LENGTH

Because there is no standard time for completion of patient caregiving assessments, the total observation time was determined based on the length of time in minutes of the caregiving assessment interval, as shown in Figure 4.2 and described below. The study video was reviewed to determine the last caregiving interaction. The time from that interaction through the observation period was designated as the pre-observation period. The observation consisted of three intervals. Timing of each interval was based on the time of interval B, with equal amounts of minutes in interval A and interval C. Interval A of the video corresponded to the time in minutes which are considered a pre-assessment or steady state. Videos were only considered if the infant had no handling or caregiving for greater than 1 minute for a minimum time equal to interval B during the pre-observation period. Interval B of the video began with a caregiver entering the incubator, completing caregiving activities, and final exit of the incubator. The caregiver exiting the incubator during interval B for brief moments (obtaining supplies, for example) was included in interval B. Interval C of the video was the post-assessment or recovery period following the caregiver's completion of the caregiving interaction and exiting the incubator. Interval A and interval C were observed for equal periods as determined by the duration of interval B. The combined total of the intervals A, B, and C resulted in a total time in minutes for the behavioral coding observation.

4.5 NOLDUS OBSERVER XT.14® PROJECT SET-UP

Noldus Observer XT.14® software can be used for video data presentation, management, and analysis (www.noldus.com/observer-xt). Behavioral or numeric analysis of behaviors, subjects, or observations can be completed. Intra- and inter-rater reliability testing can be completed within the software tool. Access to the software is password protected and enabled with a license key. User training of the Noldus Observer XT.14® software included an 8-hour hands-on training with a Noldus expert and was obtained as part of a PhD nursing elective at the UofSC College of Nursing (CON). Additional training resources included a user reference manual, online video courses, and remote consultation by technical support expert.

Within the Noldus Observer XT.14® program, a project includes three distinct phases: setup, observation, and analysis. During setup, the user enters behavior modifiers and subject information. Behaviors that cannot occur at the same time were coded as mutually exclusive, for example fisting and a finger splay cannot occur simultaneously in the same hand. The check function was used to ensure the coding scheme was free from errors. Initial errors realized were "conflicting keycodes" in the project's settings whereby the character number length was not specific. Once errors were corrected, an independent reviewer evaluated the final coding scheme entry.

Noldus Observer XT.14® software technical consultation was required several times throughout feasibility testing. One laptop hard drive failed during the testing and reinstallation of the Noldus Observer XT.14® software was required. The license token key needed to be reinstalled following the hard drive replacement. Furthermore, backup files had to be accessed to resume the feasibility testing.

4.5.1 CODING BEHAVIORS USING NOLDUS OBSERVER XT.14®

Feasibility coding took place in October 2020. To begin the observation, codes were entered into the Noldus Observer XT.14® software as anticipated behaviors. Defined by the coding scheme, behaviors relevant for this feasibility study, reflect infant stability or instability within each subsystem. The coding scheme was entered before proceeding to the video file transfer.

One purposely selected subject’s video file was transferred and stored to a separate folder on a UofSC CON regulated server, with password protection. The video was selected based on identification of a subject with quality video for each interval which occurred on DOL 3, 4, and 5. The infant’s file was labeled by subject number, date of the file, and the recording time. Video data were imported in to Noldus Observer XT.14® software. For coding the infant data, the observation settings were: offline observation; continuous-time sampling; and open-ended time. An expert reviewer then confirmed the project was entered into Noldus Observer XT.14® correctly.

Continuous coding using the behavioral codes was completed for each interval, followed by a periodic review of each interval. The program controller allowed for starting, playback, fast forward, and stopping when necessary to confirm or review infant reactions or caregiver interactions. Anecdotal data and contextual descriptions, such as positioning aids, equipment, caregiver actions seen during the observation were recorded in the free text section of the event log. Backup files were made following the completion of each recording and stored on the password-protected computer.

4.6 INTRA-RATER/INTER-RATER RELIABILITY

A second independent observer participated in the inter-rater reliability testing on two different occasions, coding their observations on a private secured video webchat. While this observer was experienced in behavioral observations using NIDCAP behaviors, they were blinded to the research question of interest. The Kappa score (κ) is frequently used to assess inter-rater reliability for nominal variables and to measure the level of agreement between coders (Hallgren, 2012). The Kappa score demonstrates replicability of the coding scheme procedure for data collection. The Kappa score was moderate (κ =.57) on the first attempt and was subsequently repeated. After two weeks and a review of the coding scheme, a second inter-rater observation resulted in an acceptable κ of .72 and .80 (Hallgren, 2012; Martin & Bateson, 2018). The observers were determined to demonstrate >70% agreement of the infant behavior observed during the one observation interval before proceeding. The variance between raters represents the observed score, not attributable to measurement error. The intra-rater reliability was performed on one observation, and the κ =.83. Considerations for reliability related to coding definitions, operational definitions, and specific interpretations of behavior were critical to reducing personal interpretation biases of infant behaviors (Haidet et al., 2009).

4.7 ANALYSIS

Video start and stop times were based on the total observation time as determined by the length of time in minutes of the caregiving assessment interval. An excel spreadsheet was created to determine the infant's elapsed time since birth, or minutes since birth (MSB), to correlate with the video relative time recording. All data in the parent study were mapped to a trajectory timeline starting with the time of each infant's birth, which is designated as 0 MSB. Aligning the relative video time with the MSB timeline determined the age in minutes of the infant.

4.8 FEASIBILITY DATA COLLECTION METHODS

Six observations were conducted on one purposely selected infant. Of the videos from DOL 1 and 2, six care assessments were identified with quality video data to conduct the feasibility of the methods pilot. The feasibility study used Noldus Observer XT.14® software and created the coding scheme to code for stable and instable behaviors.

4.9 RESULTS

The selected infant's video data were coded in 30 intermittent sessions by a single coder. Four observations were coded on DOL 1 and two observations were coded on DOL 2, for a total of six observations. These observations consisted of two nursing care assessments on the day shift (7:00 AM – 7:00 PM) and four nursing care assessments on the night shift (7:00 PM – 7:00 AM). Video data were coded in 30 to 150 minute sessions. The coding time accounted for playback, segment selection, device, computer interruptions, and necessary pauses made by the coder.

The six observation periods included recorded data during the infant's first 27 hours of life. These six observations included an actual time of 336 minutes. Coding revealed a total of 1,798 combined stability and instability behaviors. During interval A (pre-nursing care caregiving), stress behaviors were seen more than stability behaviors in each observation among the six observations. During interval B (during caregiving), stress behaviors were observed more than stable behaviors among five observations and equally in one observation. During interval C (post-nursing care), stress behaviors were observed more frequently than stable behaviors in four of the six observations. Overall, the infant was observed to have higher instability behaviors than stability behaviors for each observation. Sustained periods of behaviors representing stability were not observed within the first 27 hours of life. The coding scheme was found to be valid and reliable in categorizing behaviors into stability and instability behaviors.

4.10 CASE STUDY SUMMARY

Observational data for each of the six observations were examined independently. For example, in this one infant's case, there were a total of 131 behaviors observed. From all behaviors observed, 113/131 (86%) were coded as stress behaviors and 18/131 (14%) were coded as stable behaviors. Figure 4.4 depicts the visualization of this observation to total behaviors only. The infant displayed greater stress behaviors during intervals A (pre-nursing care) and B (during nursing care). Higher stability behaviors were observed during interval C (post-nursing care).

4.11 LIMITATIONS OF STUDY

Noise is an environmental stressor and significant variable when assessing behaviors in premature infants. Because the video data for this infant contained no sound, it was impossible to assess the infants’ reactions which were associated with environmental noise (e.g., caregiver voices or device alarms). In future studies, optimal video observation for NIDCAP type behaviors would include both visual and audible data to facilitate capturing the infants’ responses to environmental stressors, such as noise. Within the parent study, caregivers were aware of videorecording as part of the research project. It is possible that caregivers unconsciously altered their naturally occurring behaviors or interventions, such as hand containment offered during stressful periods for the infant. It is impossible to know if the effects of recording over time resulted in caregiver habituation due to the Hawthorne effect (Haidet et al., 2009). In future studies, further analysis specific to the stability and stress behaviors based on autonomic, motor, and state subsystems should be conducted.

Biases considered during the study include the researcher’s subjectivity of experiences related to NICU patients' care and behavioral observations. During observational coding, observer’s field notes included: infant positioning aids; staff activity around the incubator, which occurred near or around a coded behavior; and, periods of infant inactivity where the infant seemed "wiped out" or non-responsive to handling and manipulation.

4.12 DISCUSSION

NICU clinicians should continually monitor the EPI for early indicators of stress and instability (Harrison et al., 2004). EPI’s behavioral responses to stress are observable (Alvarez-Garcia et al., 2014). Using the coding scheme, which was developed to understand behavioral responses to the microenvironment and macroenvironment, provides a potential method to predict illness and instability and can help to better understand GA, PCA, or gender differences (Foreman et al., 2008; Thomas, 1991; Thomas et al., 2008). In the EPI, physiologic status has been found to be more often related to motor activity than stress cues (Harrison et al., 2004), however GA and developmental capabilities are important to consider based on the understanding of the Synactive Organization of Behavioral Development (Als, 1986).

Combining behavioral observations with physiologic data from standard NICU monitoring may provide important clinical information which was not previously used until after the “stabilization period” in the EPI’s first DOL. Technological methods of displaying and providing clinical decision support for clinicians can be developed to better inform clinicians of the infants’ status without increasing workload. Further analysis of event codes in relationship to point or state events may include the start and stop of nursing assessment, sleep state behaviors, and positions associated with stress or stability before and after clinical caregiving. The coding scheme can be analyzed to reveal the frequency of an infant’s behaviors which indicate stability or instability before, during, and after clinical caregiving to determine any variation in the patient's state. The coding scheme may be used to observe and analyze groups of behaviors within and between subjects. The coding scheme can also collect data on subjects of varying GA, birthweight, postnatal days of life, and gender. In future analyses, a combination of behavioral observations, including autonomic, motor, and state behaviors, and the physiologic variables of HR, RR, and ABT can precisely be aligned to infants’ age.

4.13 CONCLUSION

Results confirm the feasibility of observing stress and stability responses to caregiving in the EPI by using a behavioral coding scheme in conjunction with the

Noldus Observer XT.14® software. Additional mixed method longitudinal studies in the EPI population are necessary to better understand EPIs' responses to stressors. Such studies should integrate physiologic variables during behavioral observation. Determining similarities or differences between behavioral and physiologic indicators of stress or instability in the critical first hours of the EPI's life can strengthen clinical data collection.

TABLE 4.1 STABILITY AND STRESS BEHAVIORS

Subsystem	Stability Behaviors	Stress Behaviors
Autonomic/Visceral	Smooth respirations, stable color, stable digestion	Seizures, respiratory pauses, tachypnea, color changes, gagging, gasping, spitting up, hiccoughing, straining, tremors, startles, twitching, coughing, sneezing, yawning, sighing
Motoric	Smooth, well-modulated posture and tone, synchronous movements consisting of hand clasping, foot clasping, finger folding, hand to mouth, grasping, suck searching, sucking, handholding, holding on, tucking	Trunk, extremity, facial, motor flaccidity, “tuning out”, “gape face”, hypertonicity with hyperextension of legs sitting on air, leg bracing, arms (airplane, salute), trunk (arching, opisthotonos), squirming, finger splays, facial grimace, tongue extension; protective maneuvers (hands on face, high guard arm, fisting) or hyperflexion of trunk and extremities; frantic diffuse activity
State	Clear, robust sleep states, rhythmic robust crying, self-quieting, or consoling	Diffuse sleep or awake states with facial twitching or smiling, strained fussing or crying, diffuse arousal
Attentional	Robust alertness, shiny eyed, and facial expressions consisting of frowning, cheek softening, “OOH” face, cooing, attentional smiling	Staring, active averting, panicked or worried alertness, rapid state oscillations, irritability, crying

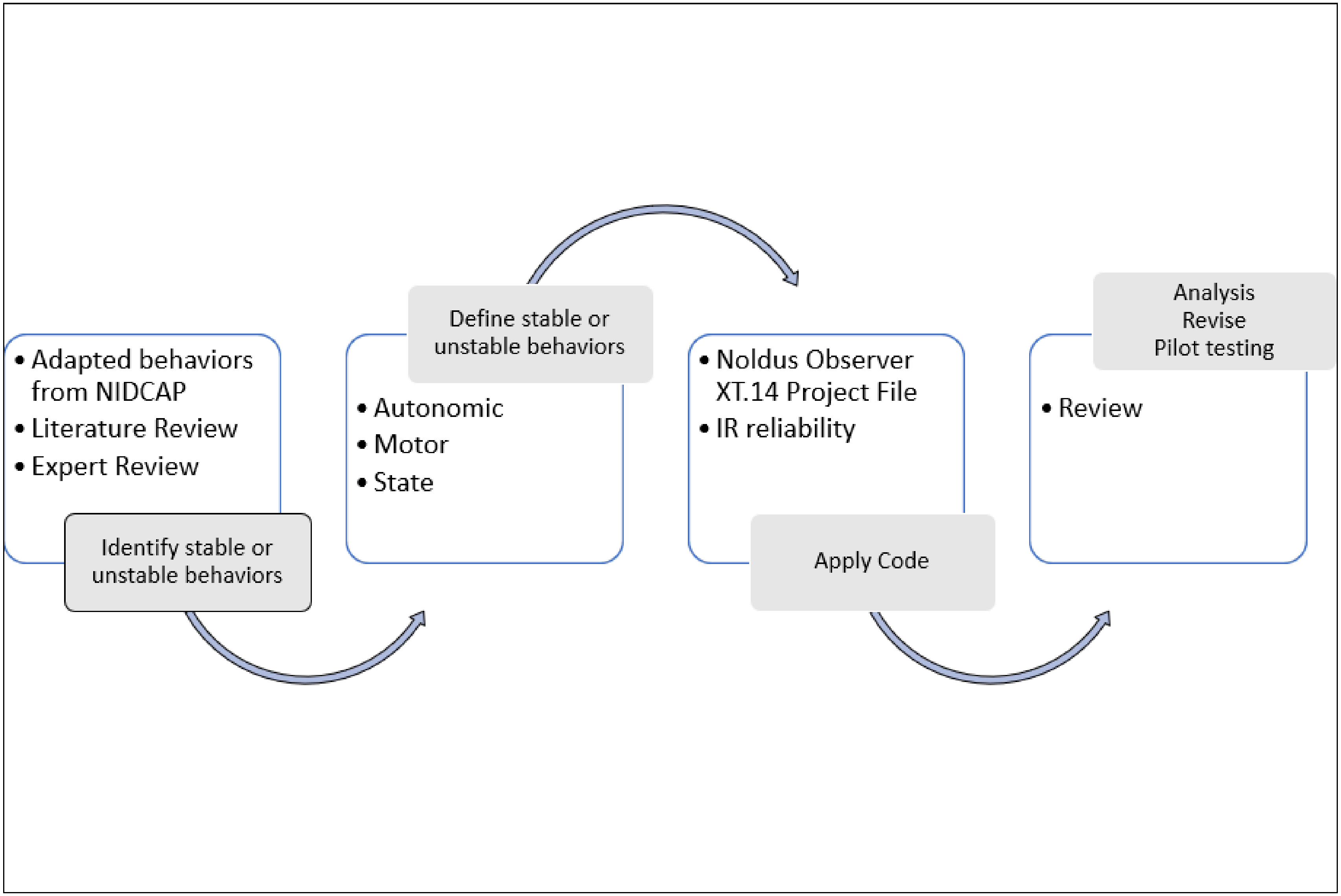

FIGURE 4.1 CODING SCHEME DEVELOPMENT ITERATIVE PROCESS

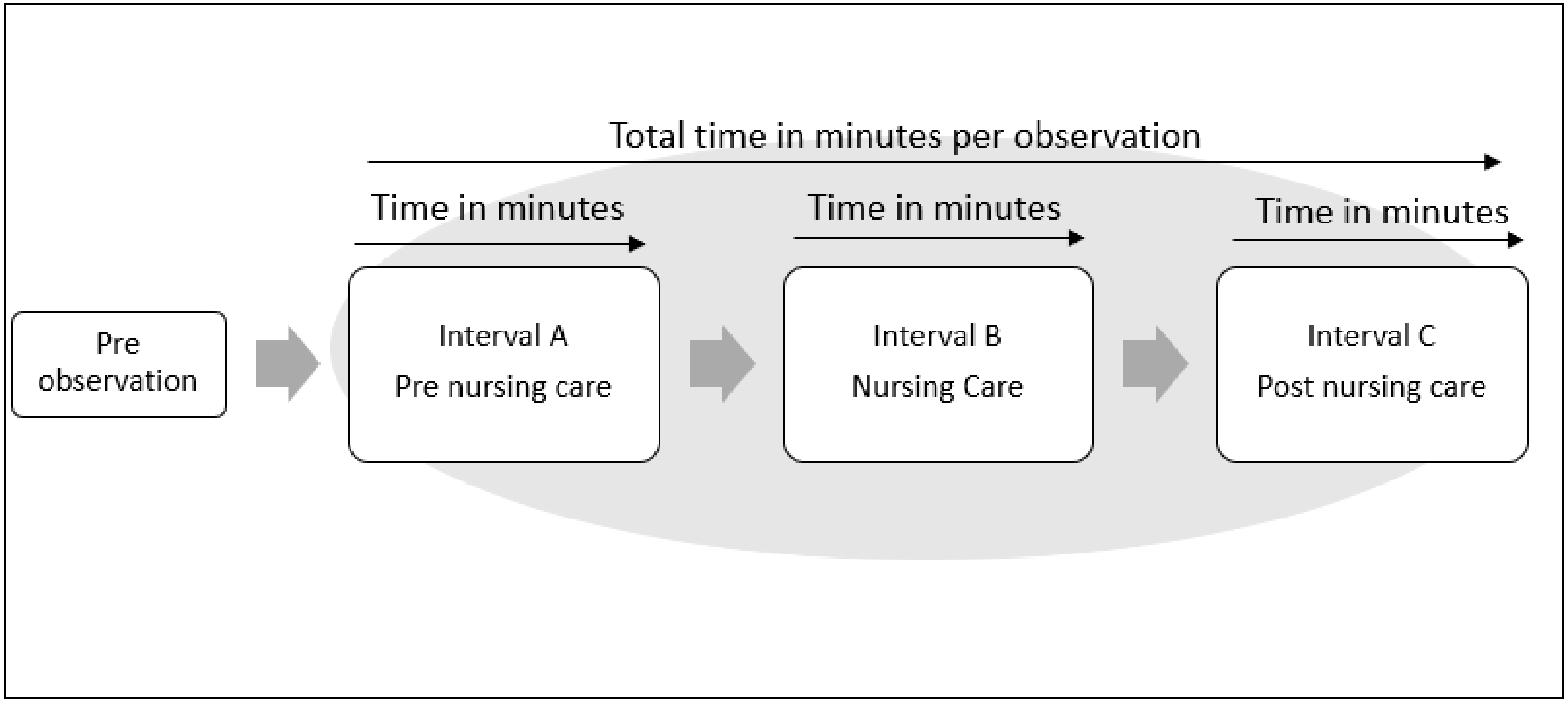

FIGURE 4.2 OBSERVATION INTERVAL TIMING

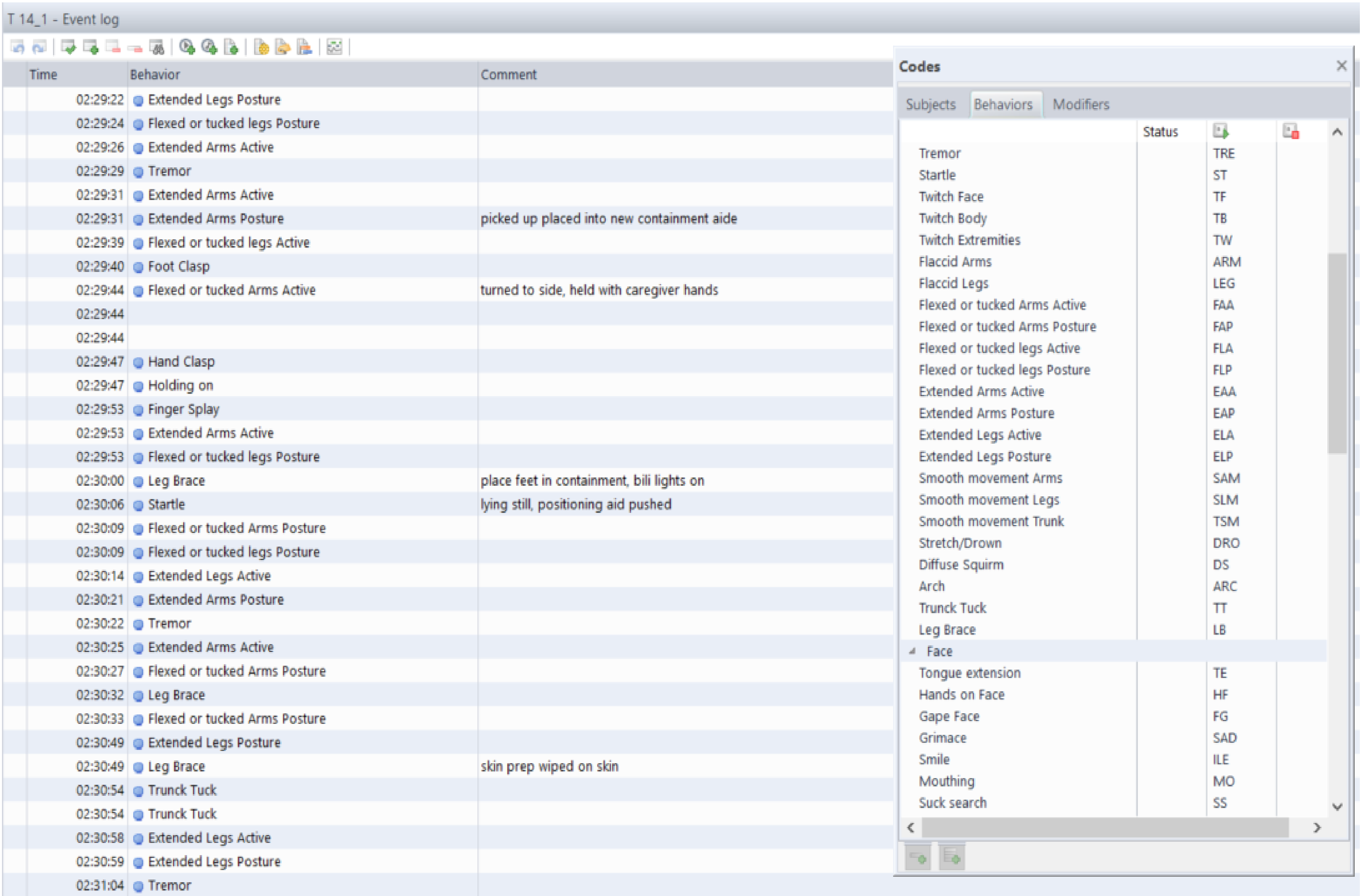

FIGURE 4.3 EVENT LOG AND CODES EXAMPLE

Observation 1 (27 mins)

Stability Behaviors
Stress Behaviors

Observation	Interval	Stability Behaviors	Stability Behaviors %	Stress Behaviors	Stress Behaviors %	Total Behaviors Observed
	A	9	14%	57	86%	66
1	B	8	13%	52	87%	60
	C	1	20%	4	80%	5
total		18	14%	113	86%	131

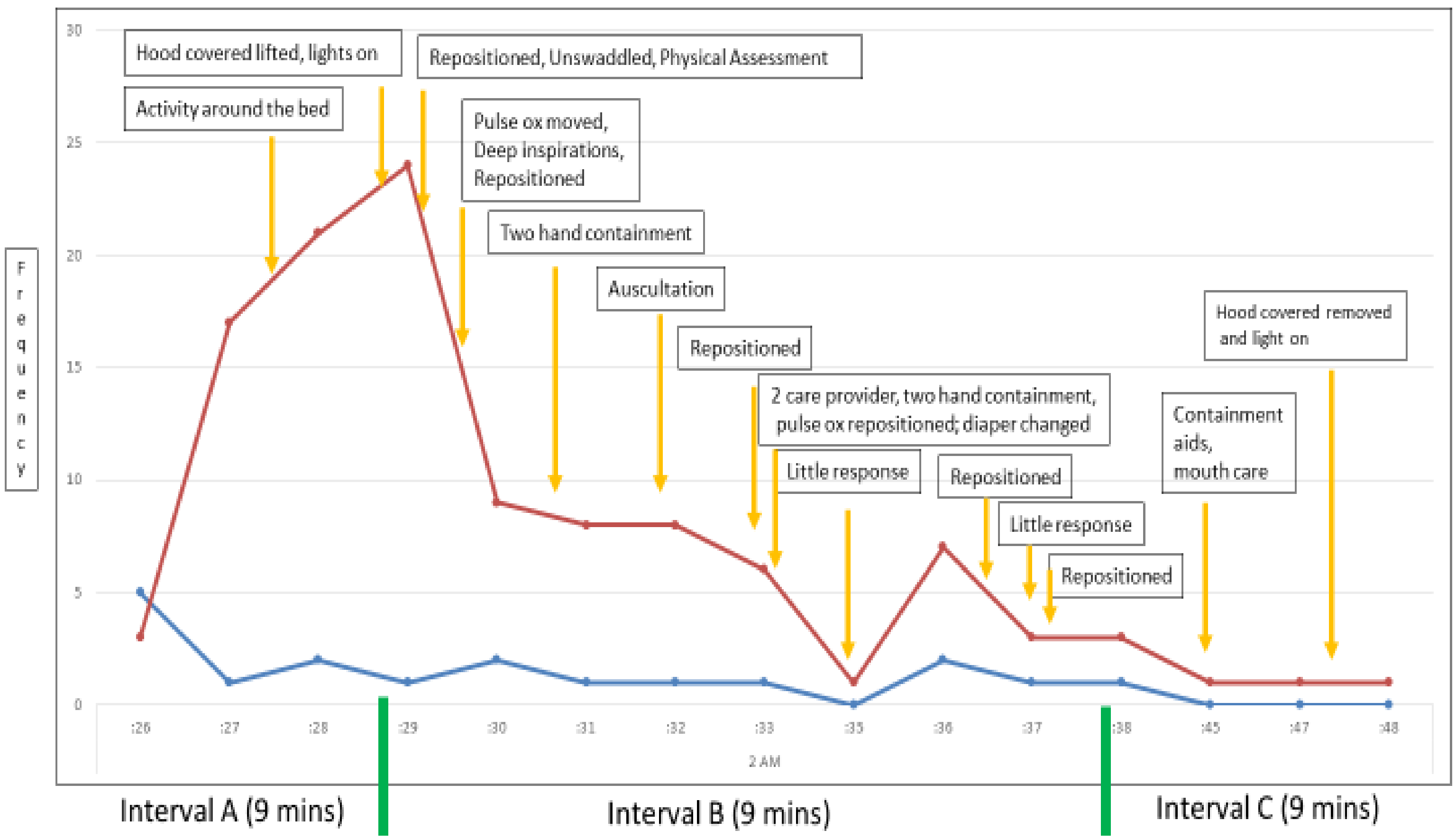

FIGURE 4.4 BEHAVORIAL OBSERVATION

CHAPTER 5

EARLY PREMATURE INFANT PHYSIOLOGIC AND BEHAVIORAL INDICATORS OF AUTONOMIC NERVOUS SYSTEM INSTABILITY STUDY RESULTS

5.1 BACKGROUND

Currently, there is a gap in scientific evidence reflecting contemporary measures of instability in the EPI. Identifying the best indicators of instability is essential to developing a clinical knowledge base and dissemination in the scientific literature. The proposed research will develop a body of knowledge that can lead to anticipatory clinical actions for identifying and preventing instability in the EPI, contributing to improved outcomes based on future interventions.

According to the U.S. National Vital Statistics reports, EPIs, those delivered before 34 completed weeks of gestation, accounted for nearly 104,000 (2.8%) of the approximately 3.7 million births in the U.S. in 2019 (Martin et al., 2019). EPIs who survive have risk of developing disabilities which can impact lifelong social, cognitive, and economic outcomes (Cheong et al., 2018; Lee et al., 2020). Chronic health care issues associated with prematurity include CLD, vision loss, hearing impairment, cerebral palsy, autism, behavioral, emotional, and social disabilities. EPIs have immature and disorganized responses to stimuli while cared for in the NICU (Modrcin-McCarthy et al., 1997). Immature and disorganized stressors from the environment, handling or stimulation, or disease states result in observable behavioral and physiologic changes, both of which reflect ANS disruption and thus instability (Als et al., 2004).

Nurses assess changes in EPIs' health statuses based on vital signs and behaviors between and during planned caregiving. The intermittent assessments and physiologic measures along with the nurse's observations of the infants change in response, activity, and color are generally reported as the infant's health status. NICU caregiving and assessments include intermittent vital sign measurements including temperature, HR, RR, and blood pressure. Additionally, routine care assessments include, infusion line assessments, respiratory care, abdominal assessments, diapering, feeding, and medical device repositioning. Caregiving and handling are known to increase stress in the EPI (Peters, 2001; Wielenga et al., 2009; Zeiner et al., 2016). Clinical decisions may be improved by earlier indicators of instability or stress throughout the EPIs NICU admission, which may lead to reduced comorbidities.

An association of abnormal thermal gradients in the EPI, represented by an increased CPTd (ABT-FT >2°C) may represent signs of infection due to ANS instability (Knobel-Dail et al., 2017). A low CPTd (ABT-FT <0°C) in the EPI has been observed with instability and a reaction to stressors (Lyon et al., 1997; Knobel-Dail, 2017). Hypothermia is defined as a BT <36.5°C (WHO, 1997) and it is an indicator of illness in the EPI and is known to increase morbidity and mortality. Abnormally low or high HRs based on GA and HR characteristics have associated comorbidities, including bradycardia, tachycardia, apnea, and suspected infection (Alonzo et al., 2018; Fairchild et al., 2013; Mithal et al., 2018). Understanding EPIs' behavioral and physiologic longitudinal responses based on ANS maturity is crucial to prevent short- and long-term comorbidities following birth (Als et al., 2004).

5.2 OBJECTIVE AND AIMS

The objective for this research is to determine if behavior or physiology, or a combination of both, is a better indicator of instability in EPIs before, during, and after nursing assessment. EPI behaviors adapted from evidenced based NIDCAP (Als, 1982; Als et al., 2005; Brazelton, 1973) behavioral observations and longitudinal physiological data will be compared. A qualitative and quantitative comparison of behavioral indicators of instability and longitudinal physiological indicators (HR, ABT, CPTd) will be examined alone and in combination of both, to determine early indicators of instability. Figure 5.1 depicts the research AIMS.

5.2.1 SPECIFIC AIM ONE

Examine infant reactions to nursing assessments between DOL 1 and 5, during the day shift and night shift for instability using a behavioral coding book derived from the traditional NIDCAP observation (model 1) shown in Figure 5.1.

5.2.2 SPECIFIC AIM TWO

Examine infant reactions to nursing assessments between DOL 1 and 5, on day shift and night shift for instability using longitudinal physiological data: HR, ABT, CPTd (model 2) shown in Figure 5.1.

5.2.3 SPECIFIC AIM THREE

Examine differences between reactions to nursing assessments between DOL 1 and 5, including instability and stability using model 1 and model 2 OR a combined assessment of model 1 and model 2 (model 3) shown in Figure 5.1.

5.2.4 SPECIFIC AIM FOUR

Compare behavioral and physiological assessments results between infants for any variation between GA, BW, gender, race, and day shift, night shifts.

5.3 DESIGN

A secondary analysis of case data (NIH/NINR: 1R15NR012157-01) from eight infants, using mixed methods and within-case analyses of 20 observation cases. Data informing each case were recorded video, longitudinal physiological data, and electronic medical record (EMR) data.

5.4 SAMPLE AND SETTING

A selection of 20 case observations was chosen to have a sample that would permit a detailed multiple case within-case analysis. Twenty case observations were generated from eight infants, who were purposely selected from the parent study to provide variation. Multiple case observations were generated from an individual infant. The selected infants allowed for case observations of intervals before, during, and after nursing assessments to vary across multiple days. Figure 5.2 depicts the multiple case within-case study design.

The selected case videos were purposely selected from parent study video recordings from DOL one through five, which allowed visualization of the infant for equal time intervals before, during, and after caregiving. The eight infants were selected for data acquisition if they had valid video and to maximize variability of GA, gender, BW, race, and PCA, with ample distribution over day and night shifts. The case observations provide the qualitative and quantitative data necessary to integrate behavioral, physiologic, and clinical context for analysis of each case.

5.5 DATA MANAGEMENT

Data for the study were obtained from the parent study which took place at a NICU in the southeast U.S. from 2010-2013 (Knobel-Dail et al., 2017; Knobel et al., 2013). The parent study included infants less than 29 weeks GA and less than 1,200 grams at birth. A video camera was positioned outside the incubator and aimed to video record study infants on DOL 1-5. Video data were stored as Mpeg files, consisting of approximately 8-12 hours of video data per file, with approximately 8-10 video files stored for each infant. Copies of these data were transferred from the institution with an IRB agreement between the parent study principal investigator’s previous institution and UofSC. IRB approval was obtained at the UofSC to use these data for this research.

During the parent study analysis, EMR data were obtained for the clinical context surrounding each infant to inform case analyses. Infant demographics (GA, BW, gender, race) and additional clinical context variables were extracted from the parent study files. Data were recorded concerning procedures and handling. These data informed the clinical context around stressors and instability for each study participant.

5.6 DATA COLLECTION

5.6.1 BEHAVIORAL VARIABLES

In the parent study, video data were recorded with a Sony video camera attached to a single pod pole attached to an incubator (Knobel et al., 2013). Prior to beginning this multiple-case study, an observational code book of behaviors (Table 5.1) was developed based on evidenced based NIDCAP behavioral assessment (Als, 1986) . Then, a methods feasibility study was conducted of six observations using video from one infant from the parent study using the finalized behavioral code book. Video data were coded using

Noldus Observer XT.14® software. After feasibility was established with a finalized behavior code book, the video files for each of the eight infants selected were coded using the video coding book. For each of the eight selected infants, video coding was completed in individual infant video project files and saved within a password protected folder on a computer. Infants' Noldus Observer XT.14® behavior software project setup included: settings for offline observation, continuous time sampling, open ended time, and no time duration. Each infants' video event coding file was then exported to password protected Excel data files.

The total observation time was determined based on the length of time in minutes of the caregiving assessment interval. The total observation included three intervals, the before (interval A), during (interval B), and after nursing care (interval C) time periods (Figure 4.2). Each interval was of equal time in minutes, which was determined based on the time of caregiver entry into the incubator and exit of the incubator. Interval A was intended to represent a resting state. Interval C was intended to represent a recovery state. Videos were only considered if the infant had no handling or caregiver entry into the incubator for greater than 1 minute during the pre-observation period, as interventions to address patient alarms or alerts are expected to occur in this population. If a less than 1 minute interaction did occur, it was recorded by the primary investigator during the observation.

As shown in Table 5.1, the coding scheme defined 110 physical-based behavioral codes based on the evidenced based newborns' autonomic, motor, and state behavioral subsystems, as described in the Model of the Synactive Organization of Behavioral Development (Als, 1982; Als et al., 1986). The autonomic subsystem includes RR, skin color, neurologic status, and visceral status (Als, 1986). The motor subsystem includes gross motor movements, facial, and extremity movements (Als, 1986). The state subsystem includes the level consciousness (sleep state) and attention-related behaviors (Als, 1986). These behaviors are reliable and valid among prematurely born infants who are cared for in the NICU (Als & McAnulty, 2011; Holsti et al., 2004; Maguire et al., 2009; Pressler, 2001).

Once coded, the case video event coding file was then exported to password protected Excel data files. The behavioral codes were divided into stability and instability, and further divided into autonomic, motor, and state subsystems.

5.6.2 PHYSIOLOGIC VARIABLES

The physiologic variables collected were ABT, CPTd, and HR. Longitudinal physiologic data files were exported from the parent study data files for each infant. Minute-to-minute data for the total observation length were saved to each case study folder.

ABT: Each file contained infant abdominal skin temperatures, measured each minute in degrees Celsius (°C), which is approximately equal to the infant's core temperature in this population (Knobel, et.al, 2013). Thermal instability is defined as an ABT < 36.5°C, or hypothermia and an ABT > 37.5°C, or hyperthermia (WHO, 1997). Thermal stability are all ABT measures not classified as hypothermia or hyperthermia.

CPTd: Each file also contained the infants' minute-to-minute FTs. The FT measures an infant's peripheral temperature. For each infant, the CPTd was a created variable using the calculation of AB-FT = CPTd. CPTd measures were also obtained every minute to correspond to the case observation interval time trajectory. This variable is indicative of the thermal gradient between the central and peripheral body. Instability of the infant using the CPTd is defined as CPTd < 0°C, meaning the peripheral body temperature is warmer than the core temperature and/or CPTd > 2°C which is an abnormally large thermal gradient between the core and periphery. A CPTd <0°C may be due to immaturity or stress (Lyon et al., 1997, Knobel-Dail et al., 2017) and > 2 °C may be due to illness or signs of infection Knobel-Dail et al., 2017).

In the parent study, AT and FT were measured by covered Y series Steri-Probe® skin temperature probes (Model 499B, Cincinnati Sub-Zero, Cincinnati, OH). These thermistor probes are accurate within ±0.2°C inside a temperature range of 34°C to 41°C (Knobel et al., 2013). All thermistors were attached to a data logger that recorded and stored temperatures to the nearest 0.1°C every minute for the study period. The temperature data loggers had calibration certificates meeting the American National Standards Institute/National Conference State Legislature requirements. During the parent study data were downloaded to a secure server and stored in a SAS dataset and were exported to password protected Excel data files for each infant. Each file contained infant abdominal skin temperature.

HR: HR measures for every minute were imported from the parent data for each observation case file for the observation duration. Premature infants have a range of HR and instability is determined as bradycardia (too low a HR) or tachycardia (too high a HR). For this study, instability and stability were determined according to the infant's GA and PCA corresponding to each case using a study of Alonzo et al. Bradycardia is the lower 5th percentile, tachycardia the 95th percentile and higher, and stability is defined as between the 5th and 95th percentiles using the chart data disseminated by these researchers

(Alonzo et al., 2018). During the parent study, infant HRs were measured every 10 seconds and recorded continually on the General Electric (GE) Healthcare cardiopulmonary and Masimo pulse oximeter bedside monitors. HR data were downloaded from the infant's monitor daily and uploaded to the infant's data file, cleaned, and averaged for one-minute intervals, then transferred to the infant's SAS data set.

5.7ANALYSES

5.7.1 WITHIN-CASE ANALYSIS

Behavioral stress and stability behaviors were qualitatively described and quantitively analyzed during each interval, changes over the interval, and between intervals. A quantitative analysis of longitudinal HR, ABT, and CPTd during each interval, changes over the interval, and between intervals was completed. A comparison was completed to determine if HR, ABT, and CPTd indicated stress or stability during the intervals. Integration of the clinical context with the behavioral and physiologic data provided details around each case. Data were synthesized and a summary conclusion was completed after data integration and synthesis for each case.

5.7.2 BEHAVIORAL ANALYSIS

The exported behavioral video files were coded for before, during, and after caregiving. The stress and stability behaviors were plotted as trends over time and visually inspected for trends. The stress and stability behaviors (Als, 1982; Brazelton, 1973) were qualitatively described and were analyzed using descriptive statistics to identify periods of instability (model 1). Descriptive statistics were used to analyze each infant's response to nursing assessments including GA, PCA, BW, gender, race, and time of observation.

5.7.3 PHYSIOLOGIC ANALYSIS

Each infant behavioral observation was coded and entered from the video data and aligned with each infants' physiologic variables by MSB. An Excel spreadsheet was created to determine the infant's elapsed time since birth, or MSB, to correlate with the video relative time recording and the physiologic data. All data in the parent study were mapped to a trajectory timeline starting with the time of each infant's birth, which was designated as 0 MSB.

The longitudinal temperature and HR Excel data files for each infant were printed as trends over time and the plotted curves were visualized for patterns before, during, and after caregiving within each case. Temperature and HR data were analyzed for descriptive analysis (model 2). Missing physiologic data in two cases was accounted for in the analysis by correcting for the minutes per interval where data were missing, (i.e., in a 10-minute observation, if 1 minute of data was missing, the calculation was based on 9 minutes).

5.7.4 COMBINED ANALYSIS

Model 1 and model 2 were then combined (model 3) and plotted as trends over time and the plotted curves were visually analyzed for trends before, during, and after caregiving within each case and longitudinally across each infant. A comparison was completed to describe the relationship between instability and HR, ABT, and CPTd differences.

5.8 RESULTS

Table 5.2 provides the selected infants' demographic information to inform cases. The 20 case observations were generated from eight infants. The GA range was 25 3/7 - 28 3/7 weeks. The BW range was 660 - 1050 grams. There were five females and two males. There were six African American (AA), one Hispanic, and one White infant. Four case observations occurred each on DOL 1, 2, and 3. Five case observations occurred on DOL 4. Three case observations occurred on DOL 5. The case observations reflected nine day shift and 11 night shift assessments. There were six infants intermittently feeding and 14 were NPO. Of the case observations which included respiratory support, six required endotracheal respiratory support and 12 required continuous positive airway pressure (CPAP) support.

5.8.1 WITHIN-CASE ANALYSES

The qualitative and quantitative within-case observation summaries for each of the 20 case observations is described and follows. Results of the within-case analysis are described for each Aim. Each case observation behavioral, physiologic, and clinical context summary is presented.

Observation 1: GA 27 5/7 weeks, AA, 880-gram, female, Apgar's 2^1 and 6^5

DOL/Observation length/shift: DOL 1, 36 minutes, day shift

Health Conditions: Prematurity; Respiratory Distress; Suspected infection; Hypothermia; Hypovolemia

Health Experiences: Maternal chorioamnionitis; Betamethasone; Potential abruption; Breech delivery; Prenatal exposure to THC and Nicotine; Surfactant/Dopamine/Epinephrine; Ventilation; Antibiotic treatment; NPO

Observation 1 Conclusion

Combined Behavioral and Physiologic Measures are shown in Figure A.1

Aim 1.

Stress and stability behaviors: There were 307 total stress and stable behaviors coded across the three intervals (263 and 44, respectively). Both the stress (before = 113, during = 90, after = 60) and stable (before = 19, during = 17, after = 8) behaviors decreased across the intervals.

Stress behaviors: Before caregiving, there were greater motor behaviors compared to autonomic or state stress behaviors (= 66 vs = 46 vs = 1, respectively). During this interval, with no caregiver interaction the infant was observed to be in an active agitated state, with kicking, squirming movements of the body and extremities and breathing responses.

During caregiving, there were greater motor behaviors compared to autonomic or state stress behaviors (= 55 vs = 28 vs = 7). A peak in the frequency of the motor stress behaviors was greatest during the caregiving period during a cluster of activity (position change, diapering, pulse checks, and auscultation). Initially, the infant was highly aroused with crying behaviors which changed to a quiet, unreactive state. Within 6 minutes of caregiving, the codable motor behaviors decreased, the infant's legs and arms laid extended and flaccid. The infant had an irregular breathing pattern, gasps, startles, and twitches more frequently during and after caregiving which are autonomic stress behaviors.

After caregiving there were greater autonomic than motor and state stress behaviors (= 33 vs = 27). No state stress behaviors were coded after caregiving. The pattern of decreasing stress behaviors across the intervals was associated with the observation of the infant remaining very still. There were decreased motor activities, irregular breathing patterns, gasps, and twitches. These behaviors may represent the infant's inability to withstand continued handling, suggesting a depletion of motor response capability and reliance of autonomic system to respond to stressors.

Stable behaviors: Before caregiving there were greater motor than state behaviors (= 17 vs = 2). During caregiving, there were greater motor than state behaviors (= 12 vs = 5). After caregiving only state behaviors were observed (= 8). The infant was with no movement within a containment device, which may have masked as the appearance of stability rather than the decrease in the infant's capability for continued motor and state stability. It is notable that no autonomic stable behaviors occurred before, during, or after caregiving which may reflect the infant's immaturity and unstable condition (ventilator support, epinephrine, and dopamine treatment) or coding error.

Aim 2.

All FTs were greater than ABTs (abnormal CPTd <0°C) which can be associated with immaturity and/or stress. The infant was hypothermic (35.0°C - 35.3°C). Direct contact with the caregiver's hands and stethoscope, in addition to opening and closing the incubator's port holes, may have contributed to hypothermia during handling and caregiving. The mean HR was normal, however it was noted that while the HR was normal for GA, the trend increased across intervals and had increased HR beat-to-beat variability during handling.

Aim 3.

Within intervals: Before caregiving, model 1 total stress and stable (86% vs 14%, respectively) behaviors and model 2 physiological measures (abnormal: CPTd, ABT; normal HR) were similar, indicating instability.

During caregiving, model 1 total stress and stable (84% vs 16%, respectively) behaviors and model 2 physiologic measures (abnormal: CPTd, ABT; normal: HR), were similar and indicate instability. After caregiving, model 1 total stress and stable behaviors (88% vs 12%, respectively) and model 2 physiologic measure (abnormal: CPTd, ABT; normal: HR), were similar and indicate instability.

Longitudinal: It is important to note the type of stress and stable behaviors varied between autonomic, motor, and stress behaviors. The infant had abnormal CPTd and ABT across all intervals. The beat-to-beat HR was normal across all intervals.

Summary: Using a combined assessment (model 3) of behavioral observations, CPTd, and ABT is a better indicator of the infant's health status across the intervals. The behavioral and physiologic indicators of instability combined with the clinical context of the infant's condition and experiences was more comprehensive than using the behavioral or physiologic indicators of instability independently. The type of stress and stability behavior coded, strengthens the interpretation of the overall stress or stable capabilities of the infant. The variables (early prematurity, race, gender, respiratory distress, hypothermia, hypotension, hypoperfusion, vasomotor control, and possible infection) may be contributors to the instability. Developmental positioning aid may be contributors to stability.

Observation 2: GA 27 5/7 weeks, AA, 880-gram, female, Apgar's 2^1 and 6^5

DOL/Observation length/shift: DOL 2, 42 minutes, night shift

Health Conditions: Prematurity; Respiratory Distress; Suspected infection; Hypothermia; Hypovolemia

Health Experiences: Maternal chorioamnionitis; Betamethasone; Potential abruption; Breech delivery; Prenatal exposure to THC and Nicotine; Dopamine; Epinephrine; Ventilation; Antibiotic treatment; NPO

Observation 2 Conclusion

Combined Behavioral and Physiologic Measures are shown in Appendix A.2

Aim 1.

Stress and stability behaviors: There were 227 total stress and stable behaviors coded across the three intervals (194 and 33, respectively). Both the stress (before = 79, during = 69, post = 46) and stable (before = 16, during = 11, post = 6) behaviors decreased across the intervals.

Stress behaviors: Before caregiving there were greater motor compared to autonomic behaviors (= 42 vs = 37). During caregiving, there were greater motor than autonomic behaviors (= 49 vs = 20). Movement around the outside of the incubator occurred when a peak in the frequency of the stress behaviors occurred before caregiving and again just prior to caregiving interval beginning. The infant was observed to have a peak of motor behaviors associated with the incubator's port hole door opening and closing, handling, diaper changing, and body position changes.

After caregiving, there were greater autonomic than motor state behaviors (= 34 vs = 12). The decreasing motor activity after caregiving seemed to represent the infant's inability to withstand continued handling, which resulted in a depletion of motor responses.

It is notable that no state behaviors were recorded before, during, or after caregiving which may reflect immaturity, or states which were not interpretable or coding errors.

Stable behaviors: Before caregiving, there were greater motor behaviors compared to autonomic or state behaviors (= 11 vs = 4 vs = 1). During caregiving, only motor behaviors were present (= 11). No autonomic or state behaviors occurred. After 5 minutes of handling, the infant decreased movement and activity. After caregiving, there were equal motor and state behaviors (= 3). There were no autonomic behaviors observed, which may have reflected the infants stressed state. Once positioned by the caregiver, the infant laid motionless, flexed, and tucked within the containment aid. The stillness observed may reflect the infant's continued stress state or a recovery from caregiving.

Aim 2.

The infant was hypothermic across all intervals (ABT <36.5°C). During caregiving, a change in incubator air temperature due to opening and closing of the portholes over 14 minutes and direct contact with cooler objects (replacement linens or diapers, caregiver's hands) may have contributed to further hypothermia. The FTs were greater than ABTs (abnormal CPTd <0°C) during the first 24 minutes of the observation. The highest HR and greatest variability of beat-to-beat HR, while normal for GA, occurred during caregiving.

Aim 3.

Within intervals:

Before caregiving, model 1 total stress and stable (83% vs 17%, respectively) behaviors and model 2 physiological measures (abnormal: CPTd, ABT; normal: HR) were similar, indicating instability.

During caregiving, model 1 total stress and stable (86% vs 14%, respectively) behaviors and model 2 physiologic measures (abnormal: CPTd, ABT; normal: HR) were similar, indicating instability.

After caregiving, model 1 total stress and stable behaviors (88% vs 12%, respectively) and model 2 physiologic measures (abnormal = ABT; normal CPTd, HR) were mixed, indicating instability and stability.

Summary: Using a combined assessment (model 3) of behavioral observations, CPTd, and ABT is a better indicator of the infant's periods of stability and instability across intervals. The behavioral and physiologic indicators of instability combined with the clinical context of the infant's condition and experiences were more comprehensive than using the behavioral or physiologic indicators of instability independently. The type of stress and stability behavior coded, strengthens the interpretation of the overall stress or stable capabilities of the infant. The PCA, race, gender, respiratory distress, hypothermia, hypotension, hypoperfusion, vasomotor control, and possible infection may each be contributors to the instability. Medical treatment, developmental positioning aids, and protection from light may have contributed to the stability.

Observation 3: GA 27 5/7 weeks, AA, 880-gram, female, Apgar's 2^1 and 6^5

DOL/Observation length/shift: DOL 3, 66 minutes, night shift

Health Conditions: Prematurity; Respiratory Distress; Suspected infection

Health Experiences: Maternal chorioamnionitis; Betamethasone; Potential abruption; Breech delivery; Prenatal exposure to THC and Nicotine; CPAP; Antibiotic treatment; NPO

Observation 3 Conclusion

Combined Behavioral and Physiologic Measures are shown in Appendix A.3

Aim 1.

Stress and stability behaviors: There were 688 total stress and stable behaviors coded across the three intervals (543 and 145, respectively). Both the stress and stable behaviors before caregiving (= 209 vs = 60, respectively), increased during caregiving (= 288 vs = 73, respectively), and decreased after caregiving (= 46 vs = 12).

Stress behaviors: Before caregiving, there were greater motor compared to autonomic behaviors (= 114 vs = 95, respectively). Prior to caregiving, it was noted that a caregiver did provide tactile stimulation one time to the infant. During caregiving there were greater motor than autonomic and state behaviors (= 206 vs = 79 vs =3, respectively). The infant had decreased observable responses to handling within 4 minutes of caregiving and appeared to be less responsive to any handling thereafter. After caregiving there were greater autonomic than motor or sleep behaviors (=29, vs = 16, vs =1). Deep intermittent sighs (an indicator of autonomic stress) and heavy abdominal breathing were observed at the end of the caregiving interaction and continued throughout the post caregiving interval.

Stable behaviors: No autonomic stable behaviors occurred before, during, or after caregiving. There were greater motor (before = 51, during = 66, after =10) compared to state behaviors (before = 9, during = 7, after = 2). After caregiving, the infant was positioned by the caregiver, supported in a flexed position within the containment aid.

Aim 2.

The BT was normal before caregiving and the infant became hypothermic (ABT <36.5°C) for 13 minutes during caregiving. The lowest ABT during caregiving was 36.2°C which may or may not be clinically significant. After caregiving, the ABT was <36.5°C for 2 minutes, likely not to be clinically significant. Entry into and exit of the incubator across the 22-minutes of caregiving and removal of the CPAP humidity may have contributed to the ABT decrease. The CPTd was within normal range (= 0 - 2°C) indicating stability. The HR was normal for GA stable across all intervals, with the highest HR occurring after caregiving. Prematurity, respiratory distress, caffeine therapy, and possible infection each may be contributors to the physiologic instability.

Aim 3.

Within intervals: Before caregiving, model 1 total stress and stable behaviors (78 vs 22%, respectively) and model 2 physiologic measures (normal: CPTd, ABT and HR) differed. Model 1 would indicate instability and model 2 would indicate stability. During caregiving, model 1 total stress and stable behaviors (80% vs 20%, respectively) and model 2 physiologic measures (normal: CPTd, HR: abnormal: ABT) differed. Model 1 would indicate instability and model 2 would indicate a mix of instability and stability. After caregiving, model 1 and model 2 total stress and stable behaviors (79%, 21%, respectively) and model 2 physiologic measures (normal: CPTd, HR, ABT) differed.

Model 1 would indicate instability and model 2 would indicate stability. The ABT temperature of <36.4°C may not be clinically significant.

Longitudinal: The longitudinal variation of total stress and stable behaviors, as well as the abnormal ABT, is important and may reflect the infant's overall instability following caregiving.

Summary: Model 3 demonstrated a more comprehensive picture of the infant's overall health status as model 2 differed across all intervals. A combined model including the clinical context of the infant's condition and experiences was more comprehensive than using the behavioral or physiologic indicators of instability independently. The infant at three days of age and had weaned to CPAP indicating improvement in their clinical condition, however, across all intervals the infant was observed to have chest wall pulling, heavy abdominal inspirations, and deep breaths (gasps). The infant initially responded with an increase in motor stress and stability behaviors which may reflect an appropriate response to handling. The infant experienced hypothermia during handling, although the clinical significance of the ABT by 0.3°C is unclear it may be an indicator of instability. One tactile stimulation of the lower extremities was provided by the caregiver for 10 seconds during the caregiving interval. The type of stress and stability behavior coded, strengthens the interpretation of the overall stress or stable capabilities of the infant. The variables of PCA, race, gender, respiratory distress, possible infection each may be contributors to the instability. Medical treatments, including caffeine as well as development care measures of positioning and protection from light may have contributed to stability.

Observation 4: GA 27 5/7 weeks, AA, 880-gram, female, Apgar's 2^1 and 6^5

DOL/Observation length/shift: DOL 4, 45 minutes, day shift

Health Conditions: Prematurity; Respiratory Distress; Suspected infection; Hyperbilirubinemia

Health Experiences: Maternal chorioamnionitis; Betamethasone; Potential abruption; Breech delivery; Prenatal exposure to THC and Nicotine; CPAP; Antibiotic treatment; NPO

Observation 4 Conclusion

Combined Behavioral and Physiologic Measures are shown in Appendix A.4

Aim 1.

Stress and stability behaviors: There were 427 total stress and stable behaviors coded across the three intervals (349 and 78, respectively). Both the stress and stable behaviors before caregiving (= 83 vs = 12, respectively) increased during caregiving (= 200 vs = 48, respectively) and decreased after caregiving (= 66 vs = 18).

Stress behaviors: Before caregiving, there were greater autonomic than motor behaviors (= 47 vs = 36, respectively). During caregiving, there were greater motor than autonomic or state behaviors (= 143 vs = 54 vs = 3, respectively). The peaks in codable stress behaviors during caregiving occurred during position changes, gastric tube insertion, diaper changes, and CPAP removal and replacement. During caregiving, the infant appeared to become flaccid, with low tone of the extremities which continued after caregiving. After caregiving there were greater autonomic than motor or state behaviors (= 44 vs = 21 vs = 1, respectively).

Stability behaviors: Before caregiving, there were greater motor than autonomic behaviors (= 11 vs = 1, respectively). During caregiving there were greater motor than state and autonomic behaviors (= 41 vs = 6 vs = 1, respectively). After caregiving there were greater motor than autonomic and state behaviors (= 10 vs = 4 vs = 4, respectively). After caregiving, it was unclear if the infant was maintaining a quiet sleep state or was continuing to recover from the stress of caregiving.

Aim 2.

Before caregiving, the infant ABT was within the normal range. The infant was hypothermic (<36.5°C) 33% of the time during caregiving and 100% of the time after caregiving. Convective and conductive heat loss may have resulted from entry into and exit of the incubator across the 15-minute caregiving interval, removal of the CPAP humidity while the CPAP was off the patient during caregiving and contact with cooler objects (multiple caregivers' hands and stethoscopes) resulting in the hypothermia. During interval A, the CPTd was above 0°C with a rise of 1.7°C after 5 minutes of caregiving. The rise in CPTd likely reflects a change in the skin temperature probe site or may reflect a perfusion changes which could be due to head position change, elevation of the body, or increased work of breathing observed. Increased HR could be expected with handling and possible discomfort associated with tape removal, handling, or management of the CPAP prongs.

Aim 3.

Within intervals: Before caregiving, model 1 total stress and stable total behaviors (87 vs 12%, respectively) and model 2 physiologic measures (normal: CPTd, ABT, HR) differed. Model 1 would indicate instability and model 2 would indicate stability.

During caregiving, model 1 total stress and stable total behaviors (81% vs 19%, respectively) and model 2 physiologic measures (intermittent abnormalities: CPTd, ABT, HR) were mixed. Model 1 would indicate instability and model 2 would indicate stability and instability.

After caregiving, model 1 total stress and stable total behaviors (79%, 21%, respectively) and model 2 physiologic measures (abnormal: CPTd, ABT, normal: HR) were mixed. Model 1 would indicate instability and model 2 would indicate stability and instability.

Longitudinal: The behavioral and physiologic responses may reflect the autonomic, motor, and state system changes and capabilities, indicating a stable infant who had increased stress during caregiving and had begun a recovery period.

Summary: Model 1 and 2 had mixed similarities and differences. The combined models, specifically including longitudinal data, provided better indicators of the infant's health status. The variables of POC, gender, race, respiratory distress, possible infection, and handling over 15 minutes may each be contributors to instability. Medical treatments, developmental positioning aids, and protection from light may have contributed to the stability.

Observation 5: GA 27 5/7 weeks, AA, 880-gram, female, Apgar's 2^1 and 6^5

DOL/Observation length/shift: DOL 5, 42 minutes, day shift

Health Conditions: Prematurity; Respiratory Distress; Suspected infection; Hyperbilirubinemia

Health Experiences: Maternal chorioamnionitis; Betamethasone; Potential abruption; Breech delivery; Prenatal exposure to THC and Nicotine; CPAP; Antibiotic treatment; Gavage Feeding

Observation 5 Conclusion

Combined Behavioral and Physiologic Measures are shown in Appendix A.5

Aim 1.

Stress and stability behaviors: There were 348 total stress and stable behaviors coded across the three intervals (238 and 110, respectively). The stress behaviors (before = 80, during = 131, post = 27) increased during caregiving from before caregiving and decreased after caregiving. The stable behaviors (before = 52, during = 52, post = 6) were the same before and during caregiving and decreased after caregiving.

Stress behaviors: Before caregiving there were greater autonomic than motor stress behaviors (= 48 vs = 32 respectively). No codable state behaviors occurred before caregiving. During caregiving there were greater motor behaviors compared to autonomic and motor behaviors (= 95 vs = 35 vs = 1, respectively). After caregiving there were greater motor behaviors compared to autonomic and state behaviors (= 16 vs = 10 vs = 1). The infant was very active and agitated at the onset of caregiving, and after 4 minutes with the CPAP removed, the infant was observed to be responding limitedly, lying with flaccid extremities. After six minutes of caregiving the infant appeared not to be responding and tactile stimulation was provided shortly thereafter. The infant was observed to remain very still, in a “frozen” state thereafter, except when behaviors increased during tape removal from the skin.

Stability behaviors: Before caregiving there were greater motor than state behaviors (= 49 vs = 3). No codable state behaviors occurred before caregiving. During caregiving there were greater motor than autonomic and state behaviors (= 48 vs = 1 vs = 3). After caregiving there were greater motor than state behaviors (= 4 vs = 2). No codable state behaviors occurred after caregiving. After caregiving, it was unclear if the infant was continuing to recover from the stress of caregiving as overall activity was low, the infant was contained within the containment aid which may have masked a sleep state in error. One period of peak of stress behaviors occurred when a caregiver quickly swabbed the infant’s mouth after caregiving.

Aim 2.

Physiologic indicators of instability across all intervals were hypothermia (<36.5C). The infant was 5 days old and the incubator set point had been increased over the previous 48 hours to 36.9°C. The infant had been extubated in the previous 24 hours which may have introduced intermittent heat loss due to CPAP removal during caregiving. Opening and closing portholes during the 14 minutes of caregiving and contact with the caregiver’s cooler hands, stethoscope, or replacement diaper may have contributed to heat loss. The CPTd variation during caregiving (between 0 - 1.5°C) may indicate a thermal gradient response to caregiving. The HR increase during handling could be expected; however, this did not occur until 8 minutes into the handling. 14% of the HR measures which were tachycardic could be related to handling. There also was missing HR data for 5 minutes before caregiving and 1 minute after caregiving. This may represent electrode disconnection or decreased adherence to the skin resulting in erroneous data.

Aim 3.

Within intervals: Before caregiving, model 1 stress and stable total behaviors (61 vs 39%, respectively) and model 2 physiologic measures (normal: CPTd, HR; abnormal ABT) were similar, both indicating a mix of instability and stability.

During caregiving, model 1 stress and stable total behaviors (72% vs 28%, respectively) and model 2 physiologic measures (intermittent abnormalities: ABT, HR, normal HR) were mixed, both indicating instability and stability.

After caregiving, model 1 stress and stable total behaviors (79%, 21%, respectively) and model 2 physiologic measures (abnormal: ABT, normal: CPTd, HR) differed. Model 1 would indicate instability and model 2 would indicate mixed instability and stability.

Longitudinal: It is important to note, the HR abnormalities occurred during the interval when there was no missing data. Additionally, the type of stress and stable behaviors varied between autonomic, motor, and stress behaviors with marked reduction in overall subsystem behaviors. These behavioral and physiologic responses may reflect the autonomic, motor, and state system changes and capabilities, indicating a stable infant who had increased stress during caregiving and remained in an unstable state following caregiving.

Summary: Model 1 and 2 had mixed similarities and differences. The combined models, specifically including longitudinal physiologic data of HR, ABT, and the type of stress and stability behaviors, provided better indicators of the infant's health status. The infant's variables of GA, phototherapy treatment (eye shields), and respiratory distress may have contributed to the instability. Feeding, containment aids, and light shielding may have contributed to the stability.

Observation 6: GA 25 3/7 weeks, AA, 950-gram, male, Apgar's 2^1 and 7^5

DOL/Observation length/shift: DOL 4, 63 minutes, day shift

Health Conditions: Respiratory Distress; Patent Ductus Arteriosus; CPAP; Hyperbilirubinemia

Health Experiences: Breech delivery; Prenatal steroids; Antibiotic treatment; Percutaneous line insertion; Gavage feeding; Phototherapy with eye shields in place

Observation 6 Conclusion

Combined Behavioral and Physiologic Measures are shown in Appendix A.6

Aim 1.

Stress and stability behaviors: There were 582 total stress and stable behaviors coded across the three intervals (472 and 110, respectively). Both the stress and stable behaviors before caregiving (= 132 vs = 29, respectively) increased during caregiving (= 209 vs = 65, respectively) and decreased after caregiving (= 131 vs = 16).

Stress behaviors: The motor behaviors were greater during caregiving (= 124) than before or after (= 51 vs = 26, respectively). The autonomic behaviors compared to before caregiving (= 81) decreased during caregiving and then increased after caregiving (= 79 vs = 105, respectively). The caregiver was observed providing tactile stimulation. During caregiving, after CPAP removal and replacement, it was not clear if the infant was bradycardic or desaturating. During caregiving, an agitated state occurred when the caregiver completed oral suction and face wiping during caregiving.

Stability behaviors: There were greater motor stability behaviors before, during, and after care giving (= 27 vs = 57 vs =13, respectively) compared to state behaviors (= 2 vs = 8 vs = 3). There were no autonomic stable behaviors coded. During the first 6 minutes of caregiving the infant was active, appearing frantic. The infant then became very still and remained so for the remainder of the observation. This may represent the infants' limited capacity to continue to support himself with protective behaviors rather than a settling and calm reaction.

Aim 2.

Before caregiving the infant was hypothermic (<36.5°C) for 14 minutes (71%) and was normothermic for 95% of the interval. After caregiving, the infant was hypothermic 24% of time. The infant remained normothermic until the last minute of the caregiving, when the temperature dropped to 36.2°C. The infant did not recover for 8 minutes into the post-caregiving interval. Opening and closing the port holes during the 21 minutes of caregiving, wiping the face, gastric lavage, and direct contact with cooler objects may have contributed to the further hypothermia during handling and caregiving. The FTs were greater than ABTs (abnormal CPTd <0°C) before caregiving 29% of the time. The CPTd was normal during and after caregiving. The abnormal thermal gradient could have been related to immaturity or a patent ductus arteriosus. The HR was normal across all intervals according to the 5 - 95% percentile for GA. The HR was stable and remained consistent until an increase near the end of caregiving and continuing after caregiving, with more variability noted. This increase may be related to handling or a reaction to an oral syringe placed in the mouth (oral mediation).

Aim 3.

Within intervals: Before caregiving, model 1 stress and stable total behaviors (82 vs 18%, respectively) and model 2 physiologic measures (intermittent abnormal: CPTd, ABT; normal: HR) differed. Model 1 would indicate instability and model 2 would indicate mixed instability and stability.

During caregiving, model 1 stress and stable total behaviors (76% vs 24%, respectively) and model 2 physiologic measures (intermittent abnormalities: ABT; normal: HR, CPTd) differed. Model 1 would indicate instability and model 2 would indicate mixed instability and stability.

After caregiving, model 1 stress and stable total behaviors (89% and 11%, respectively) and model 2 physiologic measures (abnormal: ABT; normal: CPTd, HR) differed. Model 1 would indicate instability and model 2 would indicate mixed instability and stability.

Longitudinal: The change in autonomic and motor behaviors across the intervals is interesting. These behavioral and physiologic responses may reflect the longitudinal autonomic, motor, and state system changes and capabilities, indicating a stable infant who had increased stress during caregiving and remained was returning to a recovery state following caregiving.

Summary: Model 1 and 2 had mixed similarities and differences. The combined models, specifically including longitudinal physiologic data of HR, ABT, and the type of stress and stability behaviors, provided better indicators of the infant's health status. The infant's variables of GA, phototherapy treatment (eye shields), respiratory distress, and a percutaneous line insertion the same day may have contributed to the instability. PCA, feeding, containment aids, and light shielding may have contributed to the stability.

Observation 7: GA 26 1/7 weeks, Hispanic, 660-gram, female, Apgar's 4^{1} and 7^{5}

DOL/Observation length/shift: DOL 1, 99 minutes, day shift

Health Conditions: Respiratory Distress; Hyperbilirubinemia

Health Experiences: Prenatal steroids and magnesium sulfate; Antibiotic treatment; Ventilation; Phototherapy with eye shields in place

Observation 7 Conclusion

Combined Behavioral and Physiologic Measures are shown in Appendix A.7

Aim 1.

Stress and stability behaviors: There were 348 total stress and stable behaviors coded across the three intervals (288 and 60, respectively). Both the stress and stable behaviors before caregiving (= 108 vs = 22, respectively) increased during caregiving (= 120 vs = 34, respectively) and decreased after caregiving (= 60 vs = 4).

Stress behaviors: Before caregiving there were equal motor and autonomic behaviors (= 54). There were no state behaviors coded. Before caregiving, the ventilated infant was noted to have chest wall pulling. During caregiving there were greater motor than autonomic and state behaviors (= 79 vs = 37 vs = 4). After caregiving there were greater autonomic than motor behaviors (= 51 vs = 9). There were no state behaviors coded. During caregiving the infant became very still after 27 minutes and had notable chest wall pulling. There were peaks in behaviors when the caregiver completed diapering, auscultation, and skin sensor repositioning and as a second person entered the incubator to simultaneously assesses the infant. After these caregiving activities, the infant was observed to lie very still.

Stability behaviors: Before caregiving, the motor behaviors (= 11) were greater than the state and autonomic behaviors (= 9 and = 2, respectively). During caregiving, the motor behaviors were greater (= 24) were greater than the state and autonomic behaviors (= 9 and = 2, respectively). Following caregiving the state behaviors were greater than the motor behaviors (= 3 vs =1). There were no autonomic stable behaviors coded. The decrease in stability behaviors may reflect the increased stress during caregiving for which the infant did not have ability to tolerate over time due to immaturity and/or illness.

Aim 2. The ABT was abnormal for 52% of the 33-minute caregiving interval. The extreme premature age, being less than 24 hours of age, entry into and exit of the incubator, and simultaneously having both side portholes opened at times may have all contributed to hypothermia. The incubator set point of 36.9°C and humidification may have contributed to the stability of the BT when the incubator doors were closed. The CPTd was <0°C during caregiving and reflects a thermal gradient variation related to stress and/or immaturity. The minimum HR range of 138 - 141 bpm was normal across all intervals according to the 5 - 95% percentile for GA. The mean HR increased across intervals with the highest HR during handling. The infant was observed to have heavy breathing and chest wall pulling throughout the observation reflecting respiratory instability. Physiologic changes during handling observed may reflect overall immaturity of the infant.

Aim 3.

Within intervals: Before caregiving, model 1 stress and stable total behaviors (83 vs 17%, respectively) and model 2 physiologic measures (normal: CPTd, ABT, HR) differed. Model 1 indicates instability and model 2 would indicate stability.

During caregiving, model 1 stress and stable total behaviors (78% vs 22%, respectively) and model 2 physiologic measures (intermittent abnormalities: ABT; normal: HR, CPTd) differ. Model 1 indicates instability and model 2 reflects stability and instability.

After caregiving, model 1 stress and stable total behaviors (78% and 22%, respectively) and model 2 physiologic measures (intermittent: HR; normal: CPTd, ABT) differ. Model 1 indicates instability and model 2 reflects instability and stability.

Longitudinal: The physiologic parameters varied across the intervals with intermittent CPT abnormality during caregiving and intermittent HR abnormality after care. The change in autonomic and motor behaviors across the intervals is interesting, notably the increase in autonomic and state behaviors after caregiving.

Summary: Model 1 and 2 had mixed similarities and differences. The behavioral and physiologic responses, including the longitudinal autonomic, motor, and state system changes indicate an unstable infant who had increased stress during caregiving and remained unstable following caregiving. The combined models, specifically including longitudinal physiologic data of HR, ABT, and the type of stress and stability behaviors, provided better indicators of the infant's health status. The infant's GA, PCA, gender, race, respiratory distress, possible infection, hyperbilirubinemia, discomfort, and 33 minutes of handling, prenatal steroids, and magnesium sulfate may be contributors to the instability.

Observation 8: GA 26 1/7 weeks, Hispanic, 660-gram, female, Apgar's 4^{1} and 5^{5}

DOL/Observation length/shift: DOL 2; 25 minutes, day shift

Health Conditions: Respiratory Distress; Hyperbilirubinemia

Health Experiences: Prenatal steroids and magnesium sulfate; Antibiotic treatment; Ventilation; Phototherapy with eye shields in place

Observation 8 Conclusion

Combined Behavioral and Physiologic Measures are shown in Appendix A.8

Aim 1.

Stress and stability behaviors: There were 394 total stress and stable behaviors coded across the three intervals (302 and 92, respectively). Both the stress (before = 57, during = 127, after = 118) and stable behaviors (before = 20, during = 39, after = 33) increased from before caregiving to during caregiving and then decreased from during care to after caregiving.

Stress behaviors: Before caregiving there were greater motor (= 29) than autonomic and state behaviors (= 27 vs = 1, respectively). Before caregiving, the infant appeared to be stressed and was displaying signs of respiratory disease (continued irregular respirations, chest wall pulling). During caregiving there were greater motor behaviors (= 81) than autonomic and state behaviors (= 43 vs = 3, respectively). The infant was observed to change behaviors during handling, becoming very still and remained so, after the caregiver repositioned the infant's head and body. After caregiving there were greater autonomic (= 58) than motor and state (= 56 vs = 4, respectively). Across all intervals, the infant was observed to have chest wall pulling. The infant was in a stressed, unstable state before caregiving which worsened during care giving.

Stability behaviors: Before caregiving there were greater motor than state behaviors before (= 12 vs = 8, respectively), during caregiving (= 32 vs = 7, respectively) and after caregiving (= 26 vs = 7, respectively). There were no autonomic stable behaviors in any interval. The infant did have the capability to demonstrate stable motor and state behaviors, both of which were supported by the containment aides and protection from light before and after caregiving, however, these may have been unable to contribute stability to the higher stress condition.

Aim 2.

The physiologic measures overall did not indicate instability except hypothermia (<36.5°C) for the last 3 minutes of caregiving. This may reflect loss of heat over 25 minutes while the incubator port holes were open, loss of humidity, infant handling or contact with cooler hands and medical equipment. The CPTd, while normal, narrowed overall. This represents a change in the thermal gradient which may be related to stress and /or prematurity. The HR was normal for the 5 - 95% percentile range with increased variation during and after caregiving. The maximum HR of 170 bpm occurred after caregiving, which was a change from before caregiving. This could be a result of caregiving stress due to handling, suctioning, and position changes.

Aim 3.

Within intervals: Before caregiving, model 1 stress and stable total behaviors (74 vs 26%, respectively) and model 2 physiologic measures (normal: CPTd, HR, ABT) differed. Model 1 indicates instability and model 2 indicates stability.

During caregiving, model 1 stress and stable total behaviors (77% vs 23%, respectively) and model 2 physiologic measures (intermittent abnormalities: ABT; normal: HR, CPTd) differ. Model 1 indicates instability and model 2 reflects stability and instability.

After caregiving, model 1 stress and stable total behaviors (78% and 22%, respectively) and model 2 physiologic measures (normal: CPTd, ABT, HR) differ. Model 1 indicates instability and model 2 reflects stability and instability.

Summary: Model 1 and 2 differed. The behaviors and longitudinal autonomic, motor, and state system changes indicate an unstable infant who had increased stress during caregiving and remained unstable following caregiving. The abnormal ABT would have been the only indicator of instability if solely relying on physiologic measures. Model 3 was more comprehensive than using the behavioral or physiologic indicators of instability independently. Prematurity, gender, race, respiratory distress, possible infection, hyperbilirubinemia, discomfort during a 25-minute handling time, and the NICU environment may be contributors to the instability.

Observation 9: GA 26 1/7 weeks, Hispanic, 660-gram female, Apgar's 4^1 and 5^5

DOL/Observation length/shift: DOL 3, 30 minutes, day shift

Health Conditions: Respiratory Distress; Hyperbilirubinemia

Health Experiences: Prenatal steroids and magnesium sulfate; Antibiotic treatment; Ventilation, Phototherapy with eye shields in place

Observation 9 Conclusion

Combined Behavioral and Physiologic Measures are shown in Appendix A.9

Aim 1.

Stress and stability behaviors: There were 191 total stress and stability behaviors coded across the three intervals (= 145, = 46, respectively). The stress behaviors decreased from before, during, and after caregiving(= 72 vs = 68 vs = 5, respectively). The stability behaviors before caregiving (= 16) increased during caregiving (= 22) and then decreased after caregiving (= 8).

Stress behaviors: Before caregiving, there were greater autonomic than motor behaviors (= 59 vs = 13). There were no state behaviors coded before caregiving. During caregiving there were greater motor (= 56) than autonomic or state behaviors (= 10 and = 2, respectively). After caregiving, only motor behaviors were coded (= 5).

Stability behaviors: There were greater motor than state behaviors before caregiving (= 15 vs = 1, respectively). There was greater motor than state behaviors during caregiving (= 18 vs = 4, respectively). After caregiving, there were equal motor and state behaviors (= 3) which were greater than autonomic behaviors (= 2).

It is notable that during this 10-minute caregiving observation, the infant was exhibiting stress behaviors prior to caregiving. This infant may have experienced the need for airway clearance Following suctioning the infant achieved a stable state. The caregiver began caregiving with auscultation and diaper change. The infant was suctioned for 3 minutes of the caregiving interval, which may have caused increased stress behaviors, however this may also have resulted in clearing of the airway and a subsequent reduction in activity. There was a peak of stable and stress behaviors with repositioning and a second suctioning. Both stress and stable behaviors then decreased following caregiving. The autonomic stable behaviors after caregiving may reflect stability. This infant may have experienced the need for airway clearance and following suctioning achieved a stable state.

Aim 2.

Physiologic indicators of instability were observed indicating stress during caregiving. The infant briefly became hypothermic (<36.5°C) during caregiving. The hypothermia may reflect entry into and exit of the incubator or contact with the caregiver's cooler hands, tracheal suctioning with lavage, or care items newly placed on the infant. There was no observed temperature probe repositioning. The mean HR, while normal for GA, increased during handling. The CPTd remained within the normal range across each interval with variation from 1.3 to 0.6°C in the last two minutes of caregiving. The thermal gradient variation may be related to stress from handling.

Aim 3.

Before caregiving, model 1 stress and stable total behaviors (82% vs 18%, respectively) and model 2 physiologic measures (normal: CPTd, HR, ABT) differ. Model 1 indicates instability and the model 2 reflects stability.

During caregiving, model 1 stress and stable total behaviors (71% vs 29%, respectively) and model 2 physiologic measures (normal: HR, CPTd; intermittent abnormal: ABT) differ. Model 1 indicates instability and model 2 reflects stability.

After caregiving, model 1 stress and stable total behaviors (38% and 62%, respectively) and model 2 physiologic measures (normal: CPTd, ABT, HR) differ. Model 1 indicates stability or instability and model 2 reflects stability.

Summary: Model 1 and 2 differed. The behavioral, longitudinal autonomic, motor, and state system changes indicate an unstable infant. The physiologic measures, while generally normal, appeared very flat, with little variation which may could reflect stability or instability. However, it is interesting finding that perhaps the infant in need of airway clearance, exhibited by stress behaviors which resolved after suctioning and caregiving. Prematurity, gender, race, respiratory distress, possible infection, hyperbilirubinemia, discomfort, heat loss during 10 minutes of handling time, and possible airway obstruction may be contributors to instability. Model 3 including the clinical context of the infant's condition and experiences was more comprehensive than using the behavioral or physiologic indicators of instability independently.

Observation 10: GA 27 3/7 weeks, AA, 1040-gram, male; Apgar's 6^1 and 8^5

DOL/Observation length/shift: DOL 3, 10 minutes, night shift

Health Conditions: Prolonged Premature Rupture of Membranes; Suspected infection; Hyperbilirubinemia, Multiple Gestation

Health Experiences: Prenatal betamethasone and magnesium sulfate; Antibiotic treatment; Caffeine

Observation 10 Conclusion

Combined Behavioral and Physiologic Measures are shown in Appendix A.10

Aim 1.

Stress and stability behaviors: There were 713 total stress and stable behaviors coded across the three intervals (= 489 vs = 224, respectively). Both the stress (before = 203, during = 255, after = 118) and stable behaviors (before = 90, during = 104, after = 30) increased from before caregiving to during caregiving and then decreased after caregiving.

Stress behaviors: Before caregiving, the motor behaviors (= 125) were greater than the autonomic and state behaviors (= 66 vs =12, respectively). Before caregiving it was noted that there was movement around the incubator and at one point the incubator appeared to shake which may have accounted for the infant stress behaviors. During caregiving, the motor behaviors (= 182) were greater than the autonomic and state behaviors (= 69 vs = 4, respectively). During the 35 minutes of caregiving, the infant was observed to become less responsive to caregiving and handling interval. After caregiving, the autonomic behaviors (= 24) were greater than the motor and state behaviors (= 1).

Stability behaviors: Before and during caregiving, the motor behaviors (= 60 vs = 21, respectively) were greater than the state behaviors (= 21 vs = 13, respectively). After caregiving, the state behaviors were greater than the motor behaviors (= 16 vs =14, respectively). No autonomic stable behaviors were coded in any interval. The infant was very still within the containment aid following caregiving which differed from both previous intervals. The infant's state of stability may reflect an attempt to recover from the previous intervals which did increase stress, however the infant was capabile of demonstrating appropriate responses for DOL 3 and was not requiring any respiratory support.

Aim 2.

The infant ABT was hypothermic (<36.5°) for 51% of the 35-minute caregiving period and 99% after caregiving. The variation in the ABT may be related to the temperature probe position change, which coincided with the decreased ABT 4 minutes into the caregiving, or due to the port holes opening during care. Variation in the CPTd during handling may also reflect the temperature probe position change 4 minutes into the caregiving or a thermal gradient variation due to handling, procedures, suctioning or discomfort during the first 3 minutes of caregiving. The HR was low before and after caregiving 6% and 11% of the time, respectively. During caregiving, the HR mean was the highest. The HR variation may represent a change in electrodes at 6 minutes.

Aim 3.

Before caregiving, model 1 stress and stable total behaviors (69 vs 31%, respectively) and model 2 physiologic measures (normal: CPTd, ABT; intermittent abnormal: ABT) differed. Model 1 indicates mixed stability and instability and model 2 would indicate stability.

During caregiving, model 1 stress and stable total behaviors (73% vs 27%, respectively) and model 2 physiologic measures (intermittent abnormalities: ABT, CPTd; normal HR) differed. Model 1 indicates instability and the model 2 reflects stability and instability.

After caregiving, model 1 stress and stable total behaviors (51% and 49%, respectively) and model 2 physiologic measures (intermittent abnormal: ABT, HR; normal: CPTd) were similar. Both would indicate mixed instability and stability.

Summary: Model 1 and 2 differed. Model 3 combined with the clinical context would be a more comprehensive assessment of behavioral and physiologic indicators of instability and stability. The physiologic, autonomic, motor, and state stable and stress behaviors reflect an overall stable infant. This infant was on room air, did not require respiratory support, and was receiving intermittent gavage feeding.

Observation 11: GA 27 3/7 weeks, AA, 1040-gram, male, Apgar's 6^1 and 8^5

DOL/Observation length/shift: DOL 5, 16 minutes, night shift

Health Conditions: Prolonged Premature Rupture of Membranes; Suspected infection; Hyperbilirubinemia, Multiple Gestation

Health Experiences: Prenatal betamethasone and magnesium sulfate; Antibiotic treatment; Caffeine

Observation 11 Conclusion

Combined Behavioral and Physiologic Measures are shown in Appendix A.11

Aim 1.

Stress and stability behaviors: There were 246 total stress and stable behaviors coded across the intervals (= 187, = 59, respectively). Both the stress (before = 51, during = 103, after = 33) and stable behaviors (before = 18, during = 32, after = 9) increased from before caregiving to during caregiving and then decreased from during care to after caregiving.

Stress behaviors: The motor and autonomic behaviors before caregiving (= 33 vs = 18, respectively) increased during caregiving (= 80 vs = 23). During the caregiving interval, the infant was observed to become less responsive to caregiving within 12 minutes. Following caregiving autonomic behaviors (= 32) were greater than the motor behaviors (= 1). No state stress behaviors were coded in any interval.

Stability behaviors: Before caregiving, the motor behaviors were greater than the state behaviors (= 17 and = 1, respectively). During caregiving, the motor behaviors (= 23 were greater than the state and autonomic behaviors (= 8 vs = 1, respectively). After caregiving, the motor behaviors were greater than the state behaviors (= 8 vs = 1, respectively). The infant was contained which supported a flexed position. The infant remained still after caregiving. The containment aid may have may supported the infants' stability.

Aim 2.

All ABTs remained higher than FTs, with an overall rise during and after caregiving. The CPTd remained normal (= 0 - 2°C) which may represent better vasomotor tone of the infant on DOL 5. The CPTd varied between 0.3 - 1.3°C during caregiving. The ABT probe was repositioned 5 minutes into the caregiving period and may contributed to the decreased ABT and CPTd. The HR, while 99% normal for the 5 - 95% percentile HR for GA, decreased in variation during and after handling. Decreased beat-to-beat variation may indicate stress.

Aim 3.

Before caregiving, model 1 stress and stable total behaviors (74% vs 26%, respectively) and model 2 physiologic measures (normal: CPTd, ABT, HR) differed. Model 1 indicates mixed instability and model 2 would indicate stability.

During caregiving, model 1 stress and stable total behaviors (76% vs 24%, respectively) and model 2 physiologic measures (intermittent abnormalities: ABT, HR; normal: CPTd) differed. Model 1 indicates instability and model 2 reflects generally reflects stability. The temperature probe adjustment may also reflect the ABT instability.

After caregiving, model 1 stress and stable total behaviors (79% and 21%, respectively) and model 2 physiologic measures (normal: CPTd, ABT, HR) differed. Model 1 would indicate instability and model 2 would indicate stability.

Summary: Model 1 and 2 differed. Model 3 combined with the clinical context would be a more comprehensive assessment of behavioral and physiologic indicators of instability and stability. This infant was 5 days old, did not require respiratory assistance, and was receiving gavage feeding. The stability and instability behaviors with an overall stable physiologic status represents as stable infant. While model 2 would yield the same information, model 3 would include important biomarkers of autonomic stress or stability. The physiologic, autonomic, motor, and state stable and stress behaviors reflect an overall stable infant. Variables of GA, PCA, weight, race, gender, may each be contributors to the stability and instability. Developmental measures such as light control and positioning aids may have contributed to the stability.

Observation 12: GA 27 4/7 weeks, AA, 820-gram, female, Apgar's 5^1 and 6^5

DOL/Observation length/shift: DOL 4,10 minutes, day shift

Health Conditions: Nuchal cord

Health Experiences: Prenatal betamethasone and magnesium sulfate; Antibiotic treatment; Prenatal exposure to THC and nicotine; Caffeine therapy; Hyperbilirubinemia

Observation 12 Conclusion:

Combined Behavioral and Physiologic Measures are shown in Appendix A.12

Aim 1.

Stress and stability: There were 239 total stress and stable behaviors coded across the three intervals (= 206, = 33, respectively). The stress behaviors (before = 82, during = 87, after = 37) increased from before caregiving to during caregiving, and then decreased from during care to after caregiving. The stable behaviors before and during caregiving were equal (=12) and decreased after caregiving to (= 9).

Stress behaviors: Before caregiving, the were greater autonomic behaviors than motor behaviors (= 71 vs = 11, respectively). No state behaviors were coded before caregiving. During caregiving, there were greater motor behaviors (= 71) than autonomic or state behaviors (= 15 vs = 1, respectively). Following caregiving there were greater autonomic (= 24) than motor and state behaviors (= 12 vs = 1, respectively).

Stability behaviors: Before caregiving, there were greater motor behaviors than state behaviors (= 9 vs = 3, respectively). During caregiving there were greater motor behaviors (= 71) than autonomic and state behaviors (= 15 vs = 1). After caregiving, there were greater autonomic behaviors (= 24) than motor or state behaviors (= 12 vs = 1, respectively).

The shorter, 10 minute caregiving interval, with fewer care giving activities, as well as the overall health status of the infant may have contributed to stability. The increase in motor behaviors can be expected during caregiving and may represent the infant's maturity and capability to tolerate 10 minutes of caregiving with minimal activities that occurred.

Aim 2.

FTs were higher than ABTs (CPTd <0°C) before caregiving 100% of the time and during 40% of the caregiving interval although the FTs were higher, it was very close to the ABT representing a very small gradient. After a temperature probe reposition at 2 minutes, the CPTd reversed and became normal (= 0 - 2°C) 5 minutes into the caregiving and remained normal after caregiving. The low CPTd may represent the change in temperature probe position or a thermal gradient due to stress related to position changes or observed increased chest wall pulling during caregiving. The infant was hypothermic across all intervals (<36.5°C), although the ABT consistently increased 2 minutes after the skin temperature probe was repositioned. The HR, while normal for the GA at 5-95% percentile, had little variation across all intervals. Decreased beat-to-beat variation may indicate stress, decreased electrocardiogram (ECG) lead contact with the skin or may represent the infant's maturity and capabilities to tolerate handle to caregiving.

Aim 3.

Before caregiving, model 1 stress and stable total behaviors (87% vs 13%, respectively) and model 2 physiologic measures (abnormal: CPTd, ABT; normal: HR) were similar indicating instability.

During caregiving, model 1 stress and stable total behaviors (88% vs 12%, respectively) and model 2 physiologic measures (abnormal: ABT; intermittent abnormalities: CPTd, normal HR) differed. Model 1 would indicate instability and model 2 would indicate mixed instability and stability.

After caregiving, model 1 stress and stable total behaviors (80% and 20%, respectively) and model 2 physiologic measures (abnormal: ABT; normal: CPTd, HR) differed. Model 1 would indicate instability and model 2 would indicate mixed stability and instability.

Summary: Model 1 and 2 differed both showing mixed stability and instability. Model 3 combined with the clinical context would be a more comprehensive assessment of behavioral and physiologic indicators of instability and stability. This infant was 4 days old, did not require respiratory assistance, and was receiving gavage feeding. The shorter, 10 minute caregiving interval, with fewer care giving activities, as well as the overall health status of the infant may have contributed to stability, which model 3 would indicate. The increase in motor behaviors can be expected during caregiving and may represent the infant's maturity and capability to tolerate 10 minutes of caregiving with minimal activities that occurred. The behavioral stability and instability with an overall stable physiologic status represents a stable infant. Model 3 would include important biomarkers of autonomic stress or stability related to the decreased ABT if unrelated to a temperature probe site change. Variables of GA, PCA, weight, race, gender, may each be contributors to the stability and instability. Developmental measures such as light control and positioning aids may have contributed to the stability.

Observation 13: GA 27 0/7 weeks, Caucasian, 940-gram, female, Apgar's 1^{1}, 6^{5} and 8^{10}

DOL/Observation length/shift: DOL 3, 63 minutes, night shift

Health Experiences: Twin B, Maternal Gestational Diabetes, Prenatal betamethasone, Antibiotic treatment; Respiratory Distress, Hyperbilirubinemia

Observation 13 Conclusion

Combined Behavioral and Physiologic Measures are shown in Appendix A.13

Aim 1.

Stress and stability behaviors: Both the stress (before = 79, during = 149, after = 71) and stable behaviors (before = 38, during = 71, after = 36) increased from before caregiving to during caregiving and then decreased from during care to after caregiving.

Stress behaviors: Before caregiving, autonomic behaviors were greater than motor behaviors (= 45 vs = 34). During caregiving there were greater motor behaviors than autonomic behaviors (=117 vs = 32, respectively). The infants motor stress behaviors, which increased during caregiving, were reflective of the caregiving activities which were stressful (position changes, gastric aspiration, adhesive removal from the skin, and CPAP removal and readjustment). After caregiving, there were greater autonomic stress than motor behaviors (= 60 vs = 11). No state stress behaviors were coded in any interval.

Stability behaviors: Across all intervals, there were greater motor behaviors (before = 35, during = 67, after = 33, respectively) than state behaviors (before = 3, during = 4, after = 3, respectively). No autonomic behaviors were coded in any interval. During caregiving the infant had increased stability behaviors which reflects the infant's capability for self-protection. After caregiving, the infant remained as positioned by the caregiver, within the containment device secured with low lighting.

Aim 2.

The infant was intermittently hypothermic (<36.5°C) 19% and 52% of the time during caregiving. During the 63-minute observation, the mean ABT of 36.6°C before caregiving decreased to 36.2°C. The decrease in ABT may have been related the interruption of CPAP humidity as it was intermittently removed for caregiving, opening and closing the incubator portholes, and in direct contact with cooler objects, such as the caregiver's hands or a new diaper. It should be noted the infant was lifted off the mattress twice and held close to the open port holes of the incubator. The CPTd was normal (0 - 2°C) across all intervals. The HR was abnormally low from 43-62 % of the measures in all intervals.

Aim 3.

Before caregiving, model 1 stress and stable total behaviors (68% vs 32%, respectively) and model 2 physiologic measures (intermittent abnormal: ABT, HR; normal: CPTd) were similar, indicating mixed instability and stability.

During caregiving, model 1 stress and stable total behaviors (68% vs 32%, respectively) and model 2 physiologic measures (intermittent abnormalities: ABT, HR: normal: CPTd) were similar indicating mixed instability and stability.

After caregiving, model 1 stress and stable total behaviors (66%, 34%, respectively) and model 2 physiologic measures (abnormal: ABT; intermittent abnormal HR; normal: CPTd) were similar, indicating mixed stability and instability.

Summary: Model 1 and 2 were similar with both showing mixed stability and instability. Model 3 combined with the clinical context would be a more comprehensive assessment of behavioral and physiologic indicators of instability and stability. This infant was 3 days old. Variables of GA, PCA, weight, race, gender, may each be contributors to the stability and instability. Developmental measures such as light control and positioning aids may have contributed to the stability.

Observation 14: GA 27 0/7 weeks, Caucasian, 940-gram, female, Apgar's 1^{1}, 6^{5} and 8^{10}

DOL/Observation length/shift: DOL 5, 48 minutes, night shift

Health Experiences: Twin B, Maternal Gestational Diabetes, Prenatal betamethasone, Antibiotic treatment; Respiratory Distress, Hyperbilirubinemia, CPAP

Observation 14 Conclusion

Combined Behavioral and Physiologic Measures are shown in Appendix A.14

Aim 1.

Stress and stability:

Stress and stability behaviors: There were a total of 288 total stress and stable behaviors coded across three intervals (198 and 95, respectively). Both the stress (before = 48, during = 87, after = 58) and stable behaviors (before = 30, during = 49, after = 16) increased from before caregiving to during caregiving, and then decreased from during care to after caregiving

Stress behaviors: Before caregiving, there were equal motor and autonomic behaviors (= 24). No state stress was coded before caregiving. During caregiving, the motor behaviors (= 66) were greater than autonomic or state behaviors (= 19 vs = 2, respectively). Following caregiving the autonomic behaviors were greater than the motor behaviors (= 43 vs = 15, respectively). No state stress was coded following caregiving. Before and during caregiving, the infant had periods of activity with hyperextension of the extremities which resulted in the infant nearly rolling over. During caregiving, the infant had increased motor stability behaviors which reflects the infant's capability of the developing motor maturity and capability. The state stress behaviors during caregiving, were of a highly agitated state during the first six minutes of the caregiving. The infants motor stress behaviors which increased during caregiving were reflective of the caregiving activities (body lifting off mattress, intermittent CPAP removal and replacement, diaper changes).

Stability behaviors: Before caregiving, there were greater motor (= 23) than state or autonomic behaviors (= 5 vs = 2, respectively). During caregiving, there were greater motor than state behaviors (= 45 vs = 4). After caregiving, there were greater motor (= 14) than autonomic or state behaviors which were equal (= 1). After caregiving, the infant remained securely positioned within the containment device with low lighting. It appeared as if the infant could maintain a light, steady sleep state.

Aim 2.

The infant was normothermic (>36.5°C - 39°C) in all intervals. The ABT was higher than the peripheral FT in all intervals, however, the CPTd changed from 1.5°C at the beginning of the observation to 0.5°C. The CPTd variation reflects a change in thermal gradient which may be related to stress or immaturity. The ABT remained normal but increased from 36.8°C to 37.8°C across all intervals. The infant's agitation may have increased metabolism leading to increased ABT as well as perfusion change reflected in the CPTd. The HR was abnormally low during 19% -31% of the observation across intervals. The highest mean occurred during caregiving which may reflect the infant's agitated state. The HR after caregiving decreased to lower range before the observation beginning which may reflect stress.

Aim 3.

Before caregiving, model 1 stress and stable total behaviors (62% vs 38%, respectively) and model 2 physiologic measures (intermittent abnormal: HR; normal: CPTd, ABT) were similar indicating mixed instability and stability.

During caregiving, model 1 stress and stable total behaviors (64% vs 36%, respectively) and model 2 physiologic measures (intermittent abnormalities: HR; normal: CPTd, ABT) were similar, indicating mixed instability and stability.

After caregiving, model 1 stress and stable total behaviors (78% and 22%, respectively) and model 2 physiologic measures (intermittent abnormalities: HR; normal: CPTd, ABT) were similar, indicating mixed stability and instability.

Summary: Model 1 and 2 were similar with both showing mixed stability and instability. Model 3 combined with the clinical context would be a more comprehensive assessment of behavioral and physiologic indicators of instability and stability of a premature 5-day old showing appropriate maturation in both stability and stress behaviors in response to caregiving. Variables of GA, PCA, weight, race, gender, may each be contributors to the stability and instability. Developmental measures such as light control and positioning aids may have contributed to the stability.

Observation 15: GA 27 4/7 weeks, AA, 1050-gram, female, Apgar's 9^1 and 9^5

DOL/Observation length/shift: DOL 1, 48 minutes, day shift

Health Experiences: Possible abruption; Prenatal Magnesium sulfate

Health Conditions: Prematurity, Respiratory distress, CPAP, Caffeine therapy

Observation 15 Conclusion

Combined Behavioral and Physiologic Measures are shown in Appendix A.15

Aim 1.

Stress and stability: There were 239 total stress and stable behaviors coded across the three intervals (139 and 100, respectively). Both the stress (before = 44, during = 72, after = 23) and stable behaviors (before = 41, during = 39, after = 20) increased from before caregiving to during caregiving, and then decreased from during care to after caregiving.

Stress behaviors: Before caregiving there were greater autonomic behaviors than motor behaviors (= 23 vs = 21, respectively). Before caregiving, there were peaks in stress behavior frequencies and simultaneously, the caregiver was observed raising the incubator cover as if checking on the infant, although the caregiver never entered the incubator. During caregiving there were greater motor behaviors (= 48) than autonomic or state (= 22 vs = 2, respectively). After caregiving there were greater autonomic versus motor behaviors (= 21 vs = 2, respectively). There were no state behaviors coded before or after caregiving. The bright lighting during caregiving, caregiver handling for more than 16 minutes, and discomfort from adhesive removal may have contributed to the behavioral instability.

Stability behaviors: Before caregiving there were greater motor (= 29) than state or autonomic behaviors (= 7 vs = 5, respectively). During caregiving there were greater motor than state behaviors (= 35 vs = 4, respectively). No autonomic behaviors were coded. After caregiving there were greater motor (= 12) than state or autonomic (= 5 vs = 3, respectively).

Aim 2.

Physiologic indicators of instability were observed indicating stress across all intervals. ABTs were higher than FTs 95% of the time (CPTd >0 - 2°C). A change in the CPTd during caregiving occurred at the same time as head repositioning. The infant was becoming hypothermic (<36.5°C) during handling and remained hypothermic after caregiving. Opening and closing the port holes, interruption in CPAP humidity while removed for caregiving, and direct contact with cooler hands or medical objects may have contributed to further hypothermia during handling and caregiving. The HR was abnormal for 44-81% of the observation. The HR had the greatest range during caregiving. During caregiving there were missing data for 2 minutes.

Aim 3.

Before caregiving, model 1 stress and stable total behaviors (52% vs 48%, respectively) and model 2 physiologic measures (intermittent abnormal: HR; normal: CPTd, ABT) were similar indicating mixed instability and stability.

During caregiving, model 1 stress and stable total behaviors (65% vs 35%, respectively) and model 2 physiologic measures (intermittent abnormalities: ABT; normal: CPTd, HR) were similar indicating mixed instability and stability.

After caregiving, model 1 stress and stable total behaviors (53% and 47%, respectively) and model 2 physiologic measures (abnormal: ABT; intermittent abnormal: HR; normal:

CPTd) differed. Model 1 would indicate mixed stability and instability and model 2 would indicate instability.

Summary: Model 1 and 2 were each similar both showing mixed stability and instability. Model 3 combined with the clinical context would be a more comprehensive assessment of behavioral and physiologic indicators of instability and stability of a premature 1-day old. Variables of GA, PCA, weight, race, gender, may each be contributors to the stability and instability. Developmental measures such as light control and positioning aids may have contributed to the stability.

Observation 16: GA 27 4/7 weeks, AA, 1050-gram, female, Apgar's 9^1 and 9^5

DOL/Observation length/shift: DOL 2, 63 minutes, night shift

Health Experiences: Possible abruption; Prenatal Magnesium sulfate

Health Conditions: Prematurity, Respiratory distress, Hyperbilirubinemia, CPAP, Caffeine therapy

Observation 16 Conclusion

Combined Behavioral and Physiologic Measures are shown in Appendix A.16

Aim 1.

Stress and stability behaviors: There were 405 total stress and stability behaviors coded across the three intervals (= 242, = 163, respectively). Both the stress (before = 113, during = 95, after = 34) and stable (before = 83, during = 47, after = 33) behaviors decreased across the intervals.

Stress behaviors: Before caregiving there were greater motor than autonomic behaviors (= 69 vs = 44, respectively). During caregiving, the motor behaviors were greater than the autonomic behaviors (= 69 vs = 26, respectively). Before and during caregiving, the infant had periods of agitation and hyperextension of the extremities which resulted in the infant nearly rolling over. During caregiving, the increase in behaviors observed were related to CPAP removal and replacement, diaper changes, head turning, and repositioning.

Stability behaviors: Before caregiving, the motor behaviors (= 72), were greater than the autonomic or state behaviors (= 6 vs = 5, respectively). During caregiving, the motor behaviors were greater than the autonomic behaviors (= 43 vs = 4, respectively). After caregiving, the motor behaviors were greater (= 25) than the autonomic and state behaviors (= 28 vs = 2, respectively). During caregiving, the infant demonstrated stability behaviors which reflects the infant's efforts for self-protection or self-comforting, reflecting the level of maturity. After caregiving, the infant remained as positioned by the caregiver, within the containment device secured with low lighting.

Aim 2.

The CPTd were normal (>0 - 2°C) before caregiving, with a normal thermal gradient. The FTs became higher than the ABT during caregiving and remained < 0°C after caregiving. The CPTd <0°C, can be associated with immaturity and/or stress. The ABT decreased to <36.5°C within 3 minutes of caregiving. The temperature probe was repositioned 10 minutes into caregiving which coincided with a decrease in the ABT to 33.9°C and a sharp return to 36.2°C within 1 minute. Opening and closing the porthole doors, interruption of CPAP humidity, and direct contact with the caregiver's cool hands, and equipment may have contributed decrease in ABT by 0.5°C from the beginning of the observation until the completion of the observation. There was a higher percentage (42% - 67%) of abnormally low HRs seen across the observation. It is notable that this infant was 1 day old and prenatal exposure to Magnesium Sulfate could have been related to the abnormally low HRs.

Aim 3.

Before caregiving, model 1 stress and stable total behaviors (58% vs 48%, respectively) and model 2 physiologic measures (normal: HR, CPTd, ABT) differed. Model 1 would indicate a mix of stability and instability and model 2 would indicate stability.

During caregiving, model 1 stress and stable total behaviors (67% vs 33%, respectively) and model 2 physiologic measures (intermittent abnormalities: CPTd, ABT; normal: HR) were similar indicating mixed instability and stability. It is important to note the temperature probe repositioning may be the cause in the change of CPTd and ABT. After caregiving, model 1 stress and stable total behaviors (51% and 49%, respectively) and model 2 physiologic measures (abnormal: CPTd, ABT; normal: HR) differed. Model 1 would indicate mixed instability and stability and model 2 would indicate instability.

Summary: Model 1 and 2 differed before and after caregiving and were similar during caregiving. The increased stress and stability behaviors during caregiving may be the reason for the difference between the models during caregiving. The temperature probe readjustment also occurred during caregiving. Model 3 combined with the clinical context would be a more comprehensive assessment of behavioral and physiologic indicators of instability and stability of a premature 1 day old. Variables of GA, PCA, weight, race, gender, prenatal magnesium, prenatal steroids, may each be contributors to the stability and instability. Developmental measures such as light control and positioning aids may have contributed to the stability.

Observation 17: GA 27 4/7 weeks, AA, 1050-gram, female, Apgar's 9^1 and 9^5

DOL/Observation length/shift: DOL 3, 48 minutes, night shift

Health Experiences: Possible abruption; Prenatal Magnesium sulfate

Health Conditions: Prematurity, Respiratory distress, Hyperbilirubinemia, CPAP, Caffeine therapy

Observation 17 Conclusion

Combined Behavioral and Physiologic Measures are shown in Appendix A.17

Aim 1.

Stress and stability behaviors: There were 288 total stress and stable behaviors coded across the three intervals (164 and 124, respectively). The stress (before = 64, during = 85, after = 15) and the stable (before = 37, during = 52, after = 35) behaviors increased from before caregiving to during caregiving, and then decreased from during care to after caregiving.

Stress behaviors: Before caregiving, there were greater autonomic (= 32) than motor and state behaviors (= 28 vs = 4, respectively). The infant was observed to be agitated before care giving, nearly rolling over. There was movement around the incubator and a nearby refrigerator was open and closed serval times. During caregiving, there were greater motor than the autonomic behaviors (= 61 vs = 24, respectively). No state behaviors were coded during caregiving. A suppository treatment was given 5 minutes into the caregiving interval. The infant was observed to lie still with little movement. After caregiving there were greater autonomic than motor behaviors (= 14 vs = 1, respectively). The infants increased motor and decreased autonomic stress behaviors during caregiving may reflect the caregiving activities (suppository, CPAP removal and replacement, diaper changes, and discomfort from arm constriction with a rubber band).

Stability behaviors: Before caregiving there were greater motor behaviors (= 26) than autonomic or state behaviors (= 8 vs = 3, respectively). During care giving, there were greater motor than autonomic behaviors (= 40 vs = 12, respectively). No state behaviors were coded during caregiving. After caregiving, there were greater motor (= 28) than state and autonomic behaviors (= 5 vs = 2, respectively). After caregiving, the infant remained as positioned by the caregiver, within the containment device secured with low lighting and appeared to transition nicely to a stable sleep state. The infant may have been demonstrating a return to a deeper sleep state and an appropriate recovery from caregiving.

Aim 2.

The CPTd was normal across all intervals (CPTd >0 - 2°C). The CPTd varied during handling which may reflect a thermal gradient variation due stress of body lifting, elevation of hips, or removal of the CPAP during care giving or due to immaturity. The infant ABT was >36.5°C during all intervals and remained within 0.3°C across intervals. The mean HR, while normal for GA, increased during handling across time. The HR maximum bpm occurred immediately After caregiving and then returned to near baseline of pre-caregiving interval.

Aim 3.

Before caregiving, model 1 stress and stable total behaviors (63% vs 36%, respectively) and model 2 physiologic measures (normal: HR, CPTd, ABT) differed. Model 1 would indicate a mix of stability and instability and model 2 would indicate stability.

During caregiving, model 1 stress and stable total behaviors (62% vs 38%, respectively) and model 2 physiologic measures (normal: CPTd, HR, ABT) differed. Model 1 would indicate mixed instability and stability and model 2 would indicate stability.

After caregiving, model 1 stress and stable total behaviors (30% vs 70%, respectively) and model 2 physiologic measures (normal: CPTd, ABT, HR) differed. Model 1 would indicate a mixed instability and stability and model 2 would indicate stability.

Summary: Model 1 and 2 differed. Model 1, while generally indicating stability, did also indicate periods of instability. Model 2 indicated stability. The increased stress behaviors during caregiving and the suppository may be reason for the difference between the models during caregiving. The stability is also reflected in the longitudinal changes of the autonomic, motor, and state stable and unstable behaviors reflecting the infant's maturity and stability. Variables of GA, PCA, weight, race, gender, may each be contributors to the stability and instability. Developmental measures such as light control and positioning aids may have contributed to the stability.

Observation 18: GA 27 4/7 weeks, AA, 1050-gram, female, Apgar's 9^1 and 9^5

DOL/Observation length/shift: DOL 4, 60 minutes, night shift

Health Experiences: Possible abruption; Prenatal Magnesium sulfate

Health Conditions: Prematurity, Respiratory distress, Hyperbilirubinemia, CPAP, Caffeine therapy

Observation 18 Conclusion

Combined Behavioral and Physiologic Measures are shown in Appendix A.18

Aim 1.

Stress and stability: There were 585 total stress and stable behaviors across the three intervals (= 406 vs = 179, respectively). The stress (before = 146, during = 157, after = 103) and the stable (before = 63, during = 82, after = 34) behaviors increased from before caregiving to during caregiving and then decreased from during care to after caregiving.

Stress behaviors: Before caregiving there were greater motor (= 108) than autonomic and state behaviors (= 36 vs = 2, respectively). A gastric tube was noted to be pulling between the infant's mouth and the top of the incubator for the first 10 minutes of the interval, which was then released by a caregiver. During caregiving, there were greater motor (= 125) than autonomic and state behaviors (= 30 vs = 2, respectively). After caregiving, there were greater motor than autonomic behaviors (= 53 vs = 50, respectively).

Stability behaviors: Before caregiving there were greater motor behaviors than state behaviors (= 60 vs = 3, respectively). During caregiving there were greater motor behaviors (= 125) than autonomic and state behaviors (=3 vs = 2, respectively). After caregiving, there were greater motor (= 27) than state and autonomic behaviors (= 5 vs = 2, respectively). After caregiving, the infant remained as positioned by the caregiver, within the containment device secured. The infant laid with little activity within the containment aid and was observed to transition between light sleep and transitional sleep behaviors, which may represent recovery from stress before and during caregiving. The lights were dimmed 12 minutes after caregiving, with an interesting peak in codable behaviors.

Aim 2.

Physiologic indicators of instability were observed indicating stress across all intervals. All ABTs were greater than FTs (= 0 - 2°C) before and after caregiving. There was missing data during caregiving which precedes the maximum CPTd observed during handling. The first measured CPTd after the missing data was near 3 minutes which may represent reattachment of a temperature probe after lifting. A second period of missing data occurred before completion of the caregiving interval where it was noted the pulse oximeter was moved and perhaps the skin temperature probe was also moved but not observed. The infant was hypothermic (<36.5°C) 45% of the time preceding caregiving and remained hypothermic during and after caregiving. Before caregiving, the infant's mean ABT was 36.5°C which decreased to 35.5°C during caregiving, which could be explained by a temperature probe site change or reattachment. The infant position changes and lifting may have impacted the skin temperature probe readings due to tension of the probe wire or decreased skin contact. The trend lines for both the CPTd and the ABT before and after caregiving are similar. The mean HR, while normal for GA, had the highest mean and maximum bpm during handling.

Aim 3.

Before caregiving, model 1 stress and stable total behaviors (70% vs 30%, respectively) and model 2 physiologic measures (intermittent abnormal: ABT; normal: HR, CPTd, ABT) were similar both indicating a mix of stability and instability.

During caregiving, model 1 stress and stable total behaviors (66% vs 34%, respectively) and model 2 physiologic measures (abnormal: ABT; normal: CPTd, HR) were similar both indicating mixed instability and stability.

After caregiving, model 1 stress and stable total behaviors (75% vs 25%, respectively) and model 2 physiologic measures (abnormal: ABT; normal: CPTd, HR) were similar, both indicating mixed instability and stability.

Summary: Model 1 and 2 were similar across all intervals. Model 3 would provide a more comprehensive assessment and would have potentially identified the iatrogenic gastric tube tension earlier if continuous observation were available (camera). The infants increased codable motor stress behaviors before and during caregiving were reflected in the caregiving activities which were stressful (gastric tube tension, positioning, removal of containment, oral suctioning, and face wiping). This may reflect capacity for self-protection or self-comforting. The iatrogenic tension of the gastric tube may have contributed to the increased instability before caregiving. Containment devices and swaddling may contribute to the behavioral stability.

Observation 19: GA 26 2/7 weeks, AA, 1050-gram, male, Apgar's 6^1 and 7^5

DOL/Observation length/shift: DOL 1, 114 minutes, night shift

Health Experiences: Prenatal steroids, Prolonged Premature Rupture of Membranes

Health Conditions: Prematurity, Respiratory distress, CPAP

Observation 19 Conclusion

Combined Behavioral and Physiologic Measures are shown in Appendix A.19

Aim 1.

Stress and stability behaviors: There were a total of 672 total stress and stability behaviors coded across the three intervals (407 and 265, respectively). Both the stress (before = 190, during = 187, after = 30) and stable (before = 164, during = 66, after = 35) behaviors decreased across the intervals.

Stress behaviors: Before caregiving there were greater motor than autonomic behaviors (= 175 vs = 15, respectively). No state behaviors were coded. During caregiving there were greater motor behaviors than autonomic (= 164 vs = 23, respectively). The behaviors during caregiving peaked with position changes, and oral gastric tube, insertion. After caregiving there were greater motor than autonomic behaviors (= 22 vs = 8, respectively). No state behaviors were coded in any interval.

Stability behaviors: Before caregiving there were greater motor than state behaviors (= 161 vs = 3). During caregiving there were only motor behaviors coded (= 66). No stable behaviors were coded after caregiving. The infant's stability behaviors were supported by containment which support flexion of the extremities which may have masked the infant's instability.

Aim 2. The CPTd gradient was normal (CPTd = 0 - 2°C) across intervals, however, the CPTd mean before caregiving was 1.2°C and After caregiving it had decreased to 0.5°C. The infant ABT was <36.5°C for 34% of the caregiving interval and continued to remain low after caregiving. Opening and closing port holes over 38 minutes, direct contact with the caregiver's cool hands, linens, and medical instruments may have contributed to the further hypothermia during handling and caregiving. A temperature probe repositioning or change was not noted. The mean HR, while normal for GA, had the highest mean and maximum bpm during handling.

Aim 3.

Before caregiving, model 1 stress and stable total behaviors (54% vs 46%, respectively) and model 2 physiologic measures (normal: HR, CPTd, ABT) differed, Model 1 would indicate a mix of instability and stability and model 2 would indicate stability.

During caregiving, model 1 stress and stable total behaviors (74% vs 26%, respectively) and model 2 physiologic measures (intermittent abnormal: ABT; normal: CPTd, HR) differed. Model 1 would indicate instability and model 2 would indicate a mix instability and stability.

After caregiving, model 1 stress and stable total behaviors (54% vs 46%, respectively) and model 2 physiologic measures (abnormal: ABT; normal: CPTd, HR) were similar, both indicating mixed instability and stability.

Summary: The observations after caregiving may reflect the infants age of 21 hours, intolerance of 38 minutes of caregiving, and overall unstable the health condition. Model 1 and 2 differed before and during caregiving and were similar after caregiving. Model 3 would provide a more comprehensive assessment as it is notable that for this 1 day old infant there was a lack of autonomic and state codable stability or stress behaviors. Containment devices and swaddling may contribute to the behavioral stability. Variables such as race, gender, PCA, weight, respiratory distress, hypothermia, vasomotor tone, suspected infection, development positioning and protective lighting may each be contributors to the stability and instability.

Observation 20: GA 26 2/7 weeks, AA, 1050-gram, male; Apgar's 6^1 and 7^5

DOL/Observation length/shift: DOL 2, 87 minutes, night shift

Health Experiences: Prenatal steroids, Prolonged Rupture of Membranes

Health Conditions: Prematurity, Respiratory distress, CPAP, Suspected infection

Observation 20 Conclusion

Combined Behavioral and Physiologic Measures are shown in Appendix A.20

Aim 1.

Stress and stability behaviors: There were a total of 452 total stress and stable behaviors coded across the three intervals. The stress (before = 112, during = 152, after = 24) and the stable (before = 59, during = 84, after = 20) behaviors increased from before caregiving to during caregiving and then decreased from during care to after caregiving.

Stress behaviors: Before caregiving there were greater motor than autonomic behaviors (=84 vs = 28, respectively). During caregiving there were greater motor behaviors than autonomic behaviors (= 127 vs = 25, respectively). After caregiving there were greater motor behaviors than autonomic behaviors (= 14 vs = 10).

Stability behaviors: Before caregiving there were greater motor behaviors than state behaviors (= 50 vs = 9, respectively). During caregiving there were greater motor behaviors than state behaviors (= 84 vs =1, respectively). After caregiving there were only motor behaviors (= 20). The infant stability behaviors were supported by containment, which supports flexion of the extremities, which may have masked the infant's instability.

Aim 2.

All CPTd were normal (= 0 - 2°C). The thermal gradient increased to 1.3°C during care for 0.8°C - 0.9°C means before and after cares. The CPTd was highest during handling, it is unknown if handling leads to increased blood flow and increased thermal gradients. The infant's ABT was < 36.5°C for 100% during caregiving, 90% before caregiving, and 93% after caregiving. Opening and closing the porthole door over 29 minutes and direct contact with caregiver hands and medical instruments may have contributed to the decrease in ABT to 36.2°C during handling and caregiving. The HR remained stable across intervals.

Aim 3.

Before caregiving, model 1 stress and stable total behaviors (65% vs 35%, respectively) and model 2 physiologic measures (intermittent abnormal: ABT; normal: CPTd, HR) were similar and both showed a mix of instability and stability.

During caregiving, model 1 stress and stable total behaviors (64% vs 36%, respectively) and model 2 physiologic measures (abnormal: ABT; normal: CPTd, HR) were similar and both showed a mix of instability and stability.

After caregiving, model 1 stress and stable total behaviors (55% vs 45%, respectively) and model 2 physiologic measures (intermittent abnormal: ABT; normal: CPTd, HR) were similar both indicating mixed instability and stability.

Summary: Model 1 and model 2 were similar across the intervals. The overall decrease in stable and stress behaviors indicate the instability of the infant which reflects the infants age of 24 hours, probable intolerance of 29 minutes of caregiving and overall unstable health condition. Model 3 would provide a more comprehensive assessment as it is notable that for this 2 day old infant, there was a longitudinal increase in autonomic stress behaviors. Variable such as race, gender, PCA, weight, respiratory distress, hypothermia, vasomotor tone, suspected infection, development positioning, and protective lighting may each be contributors to the stability and instability.

5.8.1.1 OVERALL SUMMARY

Within intervals, all total stress behaviors before and during caregiving were greater than stable behaviors. Following caregiving, three of the 20 case observations had greater total stable behaviors than stress behaviors. Table 5.3 shows the percentage of stable and stress autonomic, motor, and state behaviors before, during, and after caregiving, within each interval for each case observation. Prior to caregiving, the 20 case observations had a greater percentage of motor stress behaviors than autonomic stress behaviors (10 versus 8, respectively) and two case observations had equal motor and autonomic behaviors. Prior to caregiving all stable behaviors were of the motor subsystem. During caregiving, all case observations had greater percentages of motor than autonomic or state stress and stable behaviors. Following caregiving, 15 of the 20 case observations had greater percentage of autonomic stress behaviors than motor and stress behaviors (4 vs 1, respectively).

5.8.2 BETWEEN CASE ANALYSES

5.8.2.1 AIM 1 BEHAVIORAL ANALYSIS

Each case observation was evaluated by a review across the case summary results to address the aims and generate hypotheses for further study. Table 5.4 provides the total stable and stress behaviors coded across the twenty observations for the before, during, and after caregiving intervals. Table 5.5 provides total and percentage of stress and stable autonomic, motor, and state behaviors coded before, during, and after caregiving intervals.

Across the intervals, 13 of the 20 case observations had a pattern of increased stress behaviors from before caregiving to during caregiving, and a decrease in stress behaviors following caregiving. Across the intervals, the increased stress behaviors during handling were similar on night shift than day shift (seven cases vs six cases, respectively). Case observations indicated greater stress behaviors during caregiving more commonly on DOL 3 versus DOL 1 and 2 (ten cases vs one case vs two cases, respectively). Increased stress behaviors during handling were more common during CPAP treatment compared to ventilator or when no respiratory assistance was provided (seven cases vs four cases vs two cases, respectively).

Across the intervals, 14 of the 20 case observations had a pattern of increased stability behaviors from before caregiving to during caregiving and a decrease in stability behaviors following caregiving. Of these 14 cases, there was no difference in increased stability behaviors during caregiving based on night shift or day shift (seven cases night shift vs seven cases day shift, respectively). Case observations indicating greater stability behaviors with caregiving occurred more commonly after three days of age versus DOL 1 and 2 (11 cases vs one case vs two cases, respectively). Case observations with increased stress behaviors during caregiving were receiving CPAP more frequently than ventilator or those not requiring respiratory assistance (eight CPAP vs four vent vs two room air, respectively). The case observations with increased stability during handling were more commonly NPO than receiving gavage feeds (nine cases vs five cases, respectively). Across the intervals, no case observation had increased total stress behaviors or stability behaviors from during caregiving to after caregiving.

Across the intervals before and during caregiving all case observations had a greater percentage of motor stable behaviors compared to the autonomic or state behaviors. Across all intervals after caregiving, 15 of the 20 case observations had greater percentage of motor stable behaviors than autonomic or state behaviors.

Across all intervals before caregiving, eight of 20 case observations had greater percentages of motor stress behaviors compared to autonomic stress behaviors, ten cases had greater autonomic behaviors compared to motor stress behaviors and the remaining two cases had equal motor and autonomic stress behaviors. Across all intervals, during caregiving, all case observations had a greater percentage of motor stress behaviors. Across all intervals after caregiving, 15 of the 20 case observations had a greater percentage of autonomic stress behavior compared to motor or state behaviors.

Summary of behavioral responses to caregiving: EPI reactions to caregiving generally increased infant stable and stress behaviors, thus indicating stability or instability behavioral capabilities of the infants. There are differences in the type of behavioral stable and stress responses based on the infants autonomic, motor, and state system maturity. These behavioral stable and stress differences align with the Model of the Synactive Organization of Behavioral Development and the capabilities based on ascending capabilities according to GA.

5.8.2.2 AIM 2 PHYSIOLOGIC ANALYSIS

5.8.2.2.1 HEART RATE

Across intervals, the HR was normal in 12 of the 20 case observations indicating stability. In five of the 20 case observations, there were normal trends in HR and there were sporadic HR measures outside of the stable range across the intervals. In three of the 20 cases, there were abnormal (unstable) HRs across all intervals indicating instability. Abnormal HRs across all intervals occurred in three females and were more common among 27-week PCA versus 28-week PCA (two vs one, respectively). Abnormal HRs across all intervals varied by PCA (DOL 1 = 1, DOL 3 = 1, DOL 5 = 1). The HR abnormalities were in the infants with BWs ranging 650 to 940 grams. All the case observations with HR abnormalities across all intervals were in those with CPAP support and were NPO.

5.8.2.2.2 CPTd

Across intervals, the CPTd was normal in 11 of the 20 case observations indicating stability. Abnormal CPTd occurred in nine of the 20 case observations. One case observation had an abnormal CPTd across all intervals. In eight of the 20 case observations, there were sporadic periods of CPTd instability across the intervals. Of these eight case observations, all were AA and the instability occurred equally on day and night shifts (four day shift vs four night shift). The GAs varied between 25-28 weeks PCA (25 weeks =1, 27 weeks =2, 28 weeks =5). The BW ranges between 820-1,050 grams. Respiratory support was being provided during seven of the eight case observations (CPAP = 5, ventilator = 2). Feedings were being provided by gavage during three of the eight case observations and five of the eight observations were not receiving feedings. The one abnormal CPTd across all intervals was in a 27-week AA female, weighing 880 grams on DOL 1.

5.8.2.2.3 ABT

Across all intervals, the ABT was normal in two of the 20 case observations indicating stability. Across all intervals, four of the 20 case observations were hypothermic, five of the 20 case observations became hypothermic during caregiving, and in two of the 20 case observations infants became hypothermic after caregiving. No case observation had an ABT >37.4°C in any interval.

In all case observations, the physiologic data resulted in similarities and differences in longitudinal physiologic measures indicating instability and stability across intervals. The descriptive analysis of the physiologic measures is shown in Tables 5.6, 5.7, and 5.8 for each before, during, and after caregiving interval.

5.8.3 AIM 3 COMBINED ASSESSMENT ANALYSIS

Differences between reactions to nursing caregiving and assessment including stability and instability behaviors using model 1 and model 2 and a combined assessment (model 3) were analyzed. Based on a review of the behavioral observations and clinical context, data in each case was classified as stable or unstable. The physiologic data was also categorized as stable or unstable as determined by the normal and abnormal values. Table 5.9 summarizes the comparisons of the models.

Before caregiving, 11 of the 20 case observations based on behavioral analysis (model 1) and physiologic data (model 2) differed. Model 1 would indicate instability among six cases and model 2 would indicate either stability or periods of stability in 11 cases. During caregiving, 11 of the 20 models differed; model 1 indicated either stability or mixed periods of stability (10 cases vs one case, respectively) and model 2 indicated stability or mixed periods of stability (seven cases vs four cases, respectively). After caregiving, 12 of the 20 models differed; model 1 indicated stability, periods of mixed stability, and instability or instability (one case vs four cases vs seven cases, respectively) and model 2 indicated stability, periods of mixed stability, and instability or instability (three cases vs seven cases, vs two cases, respectively). It was identified that using the behavioral indicators of instability detected instability earlier in the observation than the physiologic measures.

Across intervals, model 1 and model 2 matched in all intervals for six of the 20 case observations indicating instability. Model 2 indicated stability across all intervals in three of the 20 case observations. An unexpected finding was related to three potential patient safety (near misses) which were observed during the video behavioral observation which did not correlate to the physiologic indicators.

Overall, there were differences between the behavioral and physiologic indicators of instability across intervals. Integrating the clinical context of patient illness, health conditions and the NICU environment identified instability better than behavioral and physiologic parameters in isolation (model 3). Importantly, model 3 would have detected three potential patient safety events earlier than physiologic data alone.

5.8.4 AIM 4 BETWEEN CASE COMPARISON

There was agreement between the models indicating instability in seven of the case observations. These seven cases were generated from four of the eight infants in the study. The gestational age range was 27 0/7 to 28 3/7 weeks, and there were three females and one male. The BW range was 880-1050 grams. Respiratory support provided during the case observations were more frequently CPAP than ventilator support (five versus two, respectively).

In 15 of the 20 case observations, there was increased instability of the autonomic stress behaviors following caregiving (15 of the 20 case observations). There was agreement in the identification of autonomic stress behaviors by both models in seven of the 15 case observations.

5.9 VARIABLES OBSERVED

There are many variables that were identified within each observation that may have conflicted or interfered with behavioral and physiologic measures during this study, hence the exploratory findings may not be generalizable. Prenatal exposure to steroids, magnesium sulfate, illicit drugs, tobacco, and alcohol need to be considered. Mode and indication for delivery should be accounted for in future research. The variety of caregiving activities, opening and closing the incubator doors, humidification of incubator air and respiratory gases, as well as the time to complete caregiving varies significantly. Pharmacologic treatments of dopamine, epinephrine, caffeine, antibiotics, steroids, narcotics, analgesics, and the use of oxygen need to be considered. Containment aids and the variety of methods of swaddling infants implemented by caregivers, protection from light varies from blanket covering the incubator to eye shields placed directly on the infant. There are limitations to assessing sleep states and level of pain and discomfort in the EPI. Methods of thermoregulation and devices used to support thermal needs vary.

5.10 DISCUSSION

Application of the evidenced based NIDCAP assessment behaviors to detect EPI stress and stability behaviors combined with longitudinal analysis of HR, CPTd, and ABT is novel. This multiple case within-case study design demonstrated that the examination of infant stable and stress behaviors using video-based coding schemes combined with longitudinal ABT, CPTd, and HR provided a robust assessment of the infant’s trajectory of health and experiences during nursing assessments. This design has been used by neonatal researchers to evaluate physiologic responses in the EPI related to peripheral vasoconstriction (Knobel, Holditch-Davis, Schwartz, & Wimmer Jr, 2009) and BT (Knobel-Dail et al., 2017; Knobel et al., 2010). Researchers have evaluated physiologic and parental psychosocial outcomes in EPIs in relation to the microenvironment (Johnson, 2001), SSC, and music interventions (Ettenberger et al., 2017).

In this study, EPIs demonstrated stress and stability behaviors while cared for in the NICU. Indicators of stress and stability were evaluated with an understanding that the combination of autonomic, motor, and state behavior subsystems associated with clinical context, rather than single isolated behaviors provided a comprehensive assessment (Liaw et al., 2005). In this study, EPIs demonstrated the capability to exhibit autonomic, motor, and state stress and stable behaviors prior to DOL 5. This is consistent with previous research of instability from the NICU environment, handling or stimulation and disease states based on physiologic system changes result in observable behavioral changes (Heidelise Als, 1986; Brandon & Holditch-Davis, 2005; Grunau et al., 2004; Holditch-Davis & Hudson, 1995; Holsti et al., 2004; Holsti, Grunau, Oberlander, & Whitfield, 2005; Liaw et al., 2012; Nist, 2020; Pressler, 2001). Our findings were similar to previous research which identified that as infant's overall health status improved, there was improved capacity to tolerate interactions and stable and stress behaviors demonstrated stability (Altimier & Phillips, 2013; Hoffman et al., 2019; Kommers et al., 2019). Our study underscores the need for further studies to measure stress exposure and EPI responses while cared for in the NICU (Nist, 2020).

The Model of the Synactive Organization of Behavioral Development and subsystem maturity aligns with our findings (Heidelise Als, 1986) based on the GA of the infants including. In this study, autonomic stress behaviors were more evident of the EPI health status following caregiving. Physiologic and behavioral variations in EPIs are known to reflect ANS disruption and changes in health status, leading to instability (Als & McAnulty, 2011; Alvarez-Garcia et al., 2014) however, continued need for further research to support the stability of ANS capabilities in the EPI are needed (Burtchen et al., 2019).

Physiologic biomarkers indicating stress and instability have been identified in several studies. In this study ABT and CPTd more frequently indicated instability than beat-to-beat HR. In this study, infants experienced hypothermia before and after caregiving. Preterm infants have historically been known to experience cold stress within the first few days of life (Hey & Katz, 1969; Holditch-Davis & Hudson, 1995). Even though the analyses of the temperatures correlated with World Health Organization guidelines of hypothermia, a few infants experienced 0.1°C difference between cold stress and normal temperatures which may or may not be clinically significant. Use of specific premature infant temperature ranges may be considered for future studies as some have shown an ABT temperature increasing or decreasing outside of the infant normal range, indicates hypothermia (<36.4°C) (Lyu et al., 2015). Hypothermia is known to be a cause of increased metabolism (Lei et al., 2010). In this study, caregiving included wiping the face and body with cloths which appeared dampened. Care in the NICU, such as bathing (Chamberlain et al., 2019) and handling, are known to cause iatrogenic hypothermia.

In this study intermittent and abnormal CPTd was observed reflecting thermal gradient differences. Variation in CPTd in 9 of the 20 case observations across the intervals would be consistent with findings of other researchers. CPTd during nursing procedures and thermal stress has been demonstrated in the preterm population (Mok et al., 1991). CPTd is indicative of instability and/or stress which concurs with the findings of previous studies (Knobel, Holditch-Davis, Schwartz, & Wimmer, 2009). CPTd has been related to early onset infection and signs of illness (Ussat et al., 2015; Knobel-Dail et al., 2017). Changes in thermal gradients, which can be measured by the CPTd are indicative of instability or stress reflecting vasomotor activity (Knobel-Dail et al., 2016; Knobel et al., 2013; Lyon et al., 1997). It is interesting to note that the Hispanic infant, who had the lowest BW and was unstable on DOL 1, 2, and 3 based on the combined behavioral and physiologic (model 3) and had intermittent hypothermia across the observation, did not exhibit changes in CPTd. The CPTd needs further larger, prospective studies to better understand the potential associations between EPI stress, GA, race, BW, illness, circadian patterns, and medical treatments.

Our data showed generally normal HR based on the >5% - <95% percentiles before, during, and after caregiving. Neurobehavioral assessments not requiring handling found lower mean HR, reduced odds of tachycardia, and HR instability and handling increased HR (Allinson et al., 2017). Non-pharmacologic measures, such as swaddling and maintenance of a flexed position, was shown to result in lower HR measures (Catelin et al., 2005), which is important because in our study, the infants were generally tightly swaddled in a flexed position and contained within positioning aids. Our data were analyzed using beat-to-beat HR and the normal and abnormal percentiles were based on evidenced based preterm HR ranges (Alonzo et al., 2018). The use of HRV in future studies would provide a greater understanding of changes in HRV as an indicator of instability. HRV has been shown to be an early predictor of instability and is associated with early detection of sepsis (Fairchild, 2013; Fairchild et al., 2013). Recent studies in late preterm infants relating HRV to sleep states and immature autonomic regulation may be an interesting area of future research (Burtchen et al., 2019) in the EPI.

5.10.1 STRENGTHS AND LIMITATIONS

5.10.1.1 STRENGTHS

There are several strengths of the study. The use of the evidenced based, well established behaviors based on the NIDCAP assessment (Heidelise Als, 1986) for the identification of stress and stability in premature infants is sound. A multiple subject within-case design enabled the collection of a rich descriptive and quantitative data set for analysis. The comprehensive assessment of longitudinal variables including CPTd, ABT, and HR to the behavioral observation was novel and provided hypothesis for further studies.

5.10.1.2 LIMITATIONS

This secondary data analysis has several limitations because the parent study was not designed to answer these research questions. Further prospective studies using variables to answer the research questions would be beneficial. The large number of variables make the interpretation of the data difficult; however, this is a limitation of clinical research. While the purposeful selection of infants aimed to increase variation among the study group, there were greater AAs and females in this study. It is not known if behavioral coding is more sensitive to detecting instability. Additional clinical context related to the timing of procedures, medications, and treatments prior to any observation would have further informed the case analysis and may be helpful in future studies. The inability to have awareness of sound and noise within and surrounding the incubator is a limitation; sound as an informative variable which will, in future studies, provide valuable details for a more robust qualitative and quantitative description of infants' reactions. In this study, HR was used to analyze cardiovascular instability; however, there are limits of using beat-to-beat HR as a measure of instability. Using HRV in future studies will provide a more robust measure of cardiac instability; however, there are measurement issues with continuous HRV. Inclusion of pain scores, pain medicine, sedatives, and a better understanding of oxygen delivery and SpO2 would be informative. Devices attached to the skin of a premature infant are known to become loose or dislodged leading to missing or potentially erroneous data. This limitation was minimized in the parent study by cleaning data and eliminating temperatures that were below known skin temperatures and determined to be spurious measures. Cameras used to record videos varied and in the parent study, the camera appeared to have been moved, yielding video that made the viewing angle of the infant difficult. Additionally, lighting interfered with visibility of the infant, especially when phototherapy lights were on. Future studies would benefit from an increased recording radius, to provide the full context of the activity and NICU surroundings. Identification of EPIs' sleep states based on observation is a limitation.

5.11 CONCLUSIONS

This multiple subject, within-case design study demonstrated that a combination of behavioral and physiologic parameters, including longitudinal HR, ABT measured by skin thermistors, and CPTd measured by abdominal and foot thermistors, is a better indicator of instability, rather than using the behavioral or physiologic indicators of instability independently. Incorporation of a combination of continuous longitudinal behavioral and physiologic assessments including the subsystem analysis of stress and stable behaviors, CPTd into EPI clinical care and treatment decisions should be further evaluated. Additionally, this study also found that continuous video behavioral assessments may potentially detect early indicators of patient safety events. Behavioral and physiologic combined assessments of the EPI, which incorporate continued guidance for clinicians to reduce toxic stress in the NICU, are recommended (Weber & Harrison, 2019).

Further research is needed to identify specific continuous indicators of EPI instability during the first five DOL. Prospective studies should include a combination of continuous longitudinal behavioral and physiologic assessments including the subsystem analysis of stress and stable behaviors, CPTd, and HRV into EPI clinical care and treatment decisions. Inclusion of thermal measures including heat, humidified respiratory gases, incubator humidity would have added further clinical context. Additional measures applied from the moment of birth would include, continuous ECG, RR, SpO2, and BT including both ABT and FT to determine CPTd. Incorporating contemporary measures used to evaluate preterm infant health status would include continuous measures of CPTd, near-infrared spectroscopy and HRV. It is unknown what impact that position changes, lifting, elevation of the legs or head on circulatory perfusion and if there may be a detectable variation determined by CPTd. Further studies should evaluate the optimal length of nursing caregiving and handling to minimize instability. Understanding better indicators of instability to guide individualized interactions for EPIs are needed.

Further hypotheses and research questions include: Does prenatal exposures of mediations and illicit drugs impact indicators of stability of instability in the EPI?; Are infant demographics, including race, gender, GA, PCA, and circadian rhythms, better predictors of stability and/or instability?; Is there an interaction of convective and radiant heat from incubators and respiratory devices with infant BT and CPTd that can indicate stress in the EPI?; Is HRV compared to beat-to-beat HR a better measure better indicator of instability related to stress?; Can continuous 24-hour video analysis of behavioral responses enable better detection of instability or stability and avert potential safety issues?; Is there a relationship that can be determined by continuous 24-hour monitoring between environmental sound and noise levels and EPI stress and stability?; What are the best methods for supporting the EPI in a flexed and tucked position?; and, Can EPI instability predictive models, integrating combined behavioral and physiologic measures improve outcomes?

TABLE 5.1 QUALITATIVE, QUANTITATIVE, AND DEMOGRAPHIC VARIABLES

Variable List						
Qualitative Variables						
Behavior Variables, coded by video observation	**Variable Definition**	**Variable Code**	**State Event**	**Point Event**	**Indicator of Instability**	**Indicator of Stability**
Color						
Jaundice	Yellowish appearance; yellowness of skin.	J	x		If present	Not present
Pink	Pink appearance; pink color.	PC	x		Not present	If present
Pale	Whitish, sallow appearance in parts of face, e.g., forehead, nose or mouth area, temples, or overall skin color appearance. Gray, although one hopes it is not observed, would be noted with a special comment under pale.	Pa	x		If present	Not present
Webbed	Pattern of surface blood vessels visible in the form of a net or web, often in face, neck, at times total body surface including extremities.	Web	x		If present	Not present
Red	Purple, dark hue of face parts of the face, or body surface.	R	x		If present	Not present
Dusky	Purple, dark hue of face parts of the face, or body surface.	Dus	x		If present	Not present
Blue	Cyanotic in mouth area or other areas of the face, trunk, or extremities.	Bl	x		If present	Not present
Visceral/Resp						
Spit up	Any bringing up of feeding or saliva; more than a drool is required.	SU		x	Not present	If present

Variable List						
Qualitative Variables						
Behavior Variables, coded by video observation	**Variable Definition**	**Variable Code**	**State Event**	**Point Event**	**Indicator of Instability**	**Indicator of Stability**
Gag	The infant appears to choke momentarily or gulp; the respiratory pattern is disrupted during a gag. Gags are often but not necessarily accompanied by mild mouth opening.	G		x	If present	Not present
Burp	The infant brings up air in an expiratory burst.	B		x	If present	Not present
Hiccough	The infant hiccoughs.	Hic		x	If present	Not present
BM Grunt	Bowel movement grunting or straining. The infant's face and body display straining.	BM Gru		x	If present	Not present
Sigh	The infant in- and exhales, in a breath longer and deeper than the current respiratory pattern observed.	Si		x	If present	Not present
Gasp	The infant draws in a respiration sharply or laboriously, often after a respiratory pause; the infant may not apparently complete the inspiration and does not move smoothly to the next expiration.	Gsp		x	If present	Not present
Motor						
Tremor	Jitter or trembling of arms and legs.	TRE			If present	Not present
Startle	Sudden large amplitude jumping movement of arms or trunk or legs or whole body.	St		x	If present	Not present
Twitch Face	Brief twitch of face muscle.	TF		x	If present	Not present
Twitch Body	Brief twitch of body.	TB		x	If present	Not present
Twitch Extremities	Brief twitch of arms or legs.	TE		x	If present	Not present

Variable List						
Qualitative Variables						
Behavior Variables, coded by video observation	**Variable Definition**	**Variable Code**	**State Event**	**Point Event**	**Indicator of Instability**	**Indicator of Stability**
Flaccid Arm	The tone of one or both arms is very low, and the arm(s) lie, are held, or move flaccidly or limply.	FA		x	If present	Not present
Flaccid legs	The tone of one or both legs is very low, and the leg(s) lie, are held, or move flaccidly or limply.	FL		x	If present	Not present
Flexed or tucked Arm(s) Active	Tucking in of the arm(s). This may be repetitive activity or one adjustment.	FAA		x	Not present	If present
Flexed or tucked arm(s) Posture	Maintenance of arm(s) in a tucked position.	FAP		x	Not present	If present
Flexed or tucked Leg(s) Active	Tucking in of the leg(s), whether it is then maintained or not.	FLA		x	Not present	If present
Flexed or tucked Leg(s) Posture	Maintenance of the leg(s) in a tucked position.	FLP		x	Not present	If present
Extended Arms Active	Active extension movement of one or both arms.	EAA		x	Not present	If present
Extended Arms Posture	Maintenance of arm(s) in extension either in midair or on a surface.	EAP		x	If present	Not present
Extended Legs Active	Active extension movement of one or both legs.	ELA		x	Not present	If present
Extended Legs Posture	Maintenance of leg(s) in extension either in midair or on a surface.	ELP		x	If present	Not present
Smooth movement Arms	Smooth movement of arms.	SMA		x	Not present	If present

Variable List						
Qualitative Variables						
Behavior Variables, coded by video observation	**Variable Definition**	**Variable Code**	**State Event**	**Point Event**	**Indicator of Instability**	**Indicator of Stability**
Smooth movement Legs	Smooth movement of legs.	SML		x	Not present	If present
Smooth movement Trunk	Smooth movement of trunk, smooth movement of arms, legs, or trunk, balanced in terms of extensor and flexor component.	SMT		x	Not present	If present
Stretch/ Drown	Labored stretching of the trunk, often accompanied by arm extension and at times leg extension, which is then followed by an apparent effort to move the trunk back into flexion.	SD		x	If present	Not present
Diffuse Squirm	Small writhing, wriggling motions of the trunk, often with accompanying movements of the extremities, yet not showing the labored stretching, struggling patterns of stretch/drown.	DS		x	If present	Not present
Arch	Arching of the trunk. The upper extremities may or may not extend; the legs often extend.	A		x	If present	Not present
Trunk tuck	The infant curls or tucks trunk and/or shoulders into flexion; often the infant pulls the legs up into flexion or pull the arms in simultaneously.	TT		x	Not present	If present
Leg Brace	The infant extends leg(s) and/or feet towards the edge or wall of the incubator, crib, etc., or the caregiver's hand or body, as if to stabilize, brace, and gain boundary and inhibition to	LB		x	If present	Not present

Variable List						
Qualitative Variables						
Behavior Variables, coded by video observation	**Variable Definition**	**Variable Code**	**State Event**	**Point Event**	**Indicator of Instability**	**Indicator of Stability**
	extensor movement or posture. Even if no surface is available against which the bracing is successful, efforts at apparently seeking such a surface are also marked in this category. The infant may be actively pressing one or both feet against the mattress or a blanket roll, etc.					
Face						
Tongue extension	Tongue protrudes in extension beyond the lips or extends encased in the lower lip.	TE		x	If present	Not present
Hands on face	A hand or both hands onto the face or head, or over the ears and maintains this for at least a brief, or for a prolonged period.	HF		x	Not present	If present
Gape Face	Drooping open mouth.	GF		x	If present	Not present
Grimace	Facial extension often accompanied by lip retraction and facial retraction and distortion.	G		x	If present	Not present
Smile	Smile of face, lightly upward curving of the corner(s) of the mouth.	Sml		x	Not present	If present
Mouthing	The infant makes one or several repetitive lip and/or jaw opening and closing movements.	Mo		x	Not present	If present
Suck search	Mouth searching, rooting, as if seeking something to suck on.	SS		x	Not present	If present
Sucking	Infant sucks on hand or fingers, on clothing, bedding, the caregiver's finger or mother's breast, a pacifier or other object.	SU		x	Not present	If present

Variable List						
Qualitative Variables						
Behavior Variables, coded by video observation	**Variable Definition**	**Variable Code**	**State Event**	**Point Event**	**Indicator of Instability**	**Indicator of Stability**
Extremities						
Finger splay	Fingers are extended and separated from each other.	FS		x	If present	Not present
Airplane	Arm(s) are either fully extended out to the side at approximately shoulder level or upper and lower arm are at an angle and are extended out at the shoulder.	AP		x	If present	Not present
Salute	Arm(s) are fully extended into midair in front of the infant, either singly or simultaneously.	SLT		x	If present	Not present
Sitting on air	Legs are extended into midair either singly or simultaneously.	SOA		x	If present	Not present
Hand clasp	Infant grasps one hand with the other or clutches the hands in midline to the body.	HC		x	Not present	If present
Foot clasp	Infant positions one foot against the other, either foot sole to foot sole or one-foot sole against the other ankle or leg, or the infant folds the legs in a crossed position with feet grasping the legs or resting against them.	FC		x	Not present	If present
Hand to mouth	Infant attempts to bring one or both hands and fingers to the mouth in an apparent effort to suck on them.	HM		x	Not present	If present
Grasping	Grasping movements with the hands, either directed at the face or body, or in midair, or to the caregiver's hands or fingers or body, the	GRP		x	If present	Not present

Variable List						
Qualitative Variables						
Behavior Variables, coded by video observation	**Variable Definition**	**Variable Code**	**State Event**	**Point Event**	**Indicator of Instability**	**Indicator of Stability**
	infant's own bottle, tubing or bedding, the side of the incubator or bassinet, etc.					
Holding on	Holding on to the examiner's hands or finger or arm.	HO		x	Not present	If present
Fisting	Flexing the fingers and forming a fist.	FST		x	If present	Not present
Attention						
Yawn	The infant opens the mouth widely, usually with a deep inspiration.	Y		x	If present	Not present
Sneeze	Explosive, spasmodic action observed of face.	SN		x	If present	Not present
Face open	Infant lifts eyebrows up and extends the forehead upward.	FO		x	If present	Not present
Eyes floating	Infant's eyes move in floating, apparently disinhibited fashion, often semi-open eye position or with fully open eyes.	EF		x	If present	Not present
Avert	Infant actively looks away from a social or inanimate target.	AV		x	If present	Not present
Frown	Pulling together of the eyebrows or darkening of the eyes by squeezing of eye orbits.	FR		x	If present	Not present
Ooh face	The infant rounds the mouth and purses the lips or extends them forward in an ooh configuration.	Ooh		x	Not present	If present
Locking	Staring or eyes locking on an object.	LK		x	Not present	If present
Speech movement	The infant's tongue and lips move in soft, rhythmical, speech-like fashion.	SM		x	Not present	If present

Variable List						
Qualitative Variables						
Behavior Variables, coded by video observation	**Variable Definition**	**Variable Code**	**State Event**	**Point Event**	**Indicator of Instability**	**Indicator of Stability**
Posture						
Prone	Lying face down.	P	x		NA	NA
Side	Laying on side.	SD	x		NA	NA
Supine	Laying face up.	SP	x		NA	NA
Head						
Right	Head direction of the face towards the right.	R		x	NA	NA
Left	Head direction of the face towards the left.	L		x	NA	NA
Middle	Head direction of the face in the middle.	M		x	NA	NA
State						
Deep Sleep	Deep sleep with regular breathing or breathing in synchrony with only the respirator, eyes closed, no eye movements under closed lids; quiet facial expression; no spontaneous activity; typically, poor color.	1A	x		If present	Not present
Deep Sleep	Regular breathing: eyes closed, no eye movements under closed lids, relaxed facial expression; no spontaneous activity except isolated startles.	1B	x		Not present	If present
Light Sleep	Light sleep with eyes closed rapid eye movements may be observed under closed lids. Occasional diffuse and disorganized movements; respirations are irregular and there are many sucking and mouthing movements, whimpers; facial, body, and extremity	2A	x		If present	Not present

Variable List						
Qualitative Variables						
Behavior Variables, coded by video observation	**Variable Definition**	**Variable Code**	**State Event**	**Point Event**	**Indicator of Instability**	**Indicator of Stability**
	twitching's, much grimacing; the impression of a diffuse state is given. Color is typically poor.					
Light Sleep	Robust light sleep with eyes closed; rapid eye movements may be observed under closed lids; low activity level with movements and dampened startles. Respirations are more regular, mild sucking and mouthing movements may occur off and on; one or two whimpers may be observed, as well as infrequent sighs or smiles.	2B	x		Not present	If present
Transition state- Drowsy	Drowsy, semi-awake or semi-asleep; eyes may be open or closed, eyelids fluttering or blinking very exaggeratedly. Activity level is variable, with or without interspersed, startles from time to time; diffuse movement.	3A	x		Not present	If present
Awake- quietly awake or alert	Awake and alert, engaged.	4A	x		Not present	If present
Awake- quietly awake or alert	Appears to be staring, looking through objects, minimal activity.	4AL	x		Not present	If present
Awake- quietly awake or alert	Wide open staring eyes, looks fearful.	4AH	x		If present	Not present
Awake- quietly awake or alert	Robustly alert with bright shiny eyes, animated facial expression.	4B	x		Not present	If present

Variable List						
Qualitative Variables						
Behavior Variables, coded by video observation	**Variable Definition**	**Variable Code**	**State Event**	**Point Event**	**Indicator of Instability**	**Indicator of Stability**
Actively awake and aroused	Infant is clearly awake and aroused with distressed facial expression, grimacing, or other signs of discomfort.	5A	x		If present	Not present
Actively awake and aroused	Appears to be at the onset of vigorous cry.	5B	x		If present	Not present
Highly aroused, agitated, upset, and/or crying	Appears to be crying, cry face or upset.	6A	x		If present	Not present
Clinical Context Variables						
Behavior Variables, coded by video observation	**Variable Definition**	**Variable Code**	**State Event**	**Point Event**	**Indicator of Instability**	**Indicator of Stability**
Incubator (cover on, cover off)	Incubator (cover on, cover off).	INC	NA	NA	NA	NA
Position of body (Supine, Prone, Sideling	Position of body (Supine, Prone, side lying.	POS S, POS P POS S	NA	NA	NA	NA
Position of head (Right, Left, Middle)	Position of head (Right, Left, Middle).	HR, HL, HM	NA	NA	NA	NA
Assisted respiratory support	Respiratory Support (Nasal Cannula, CPAP, Ventilator, None).	NC, CPAP, V, None)	x		If present	Not present

Variable List						
Qualitative Variables						
Behavior Variables, coded by video observation	**Variable Definition**	**Variable Code**	**State Event**	**Point Event**	**Indicator of Instability**	**Indicator of Stability**
Diagnoses	Diagnoses (Prematurity, Respiratory Distress, Infection, PDA, Apnea, Bradycardia, Seizures, Hypothermia, Hyperthermia, Jaundice, Hyperbilirubinemia NEC, PDA).		NA	NA	NA	NA
Day 3, AM shift interval	Day 3, AM shift interval.	D3AM	NA	NA	NA	NA
Day 3, PM shift interval	Day 3, PM shift interval.	D3PM	NA	NA	NA	NA
Day 4, AM shift interval	Day 4, AM shift interval.	D4AM	NA	NA	NA	NA
Day 4, PM shift interval	Day 4, PM shift interval.	D4PM	NA	NA	NA	NA
Day 5, AM shift interval	Day 5, AM shift interval.	D5AM	NA	NA	NA	NA
Day 5, PM shift interval	Day 5, PM shift interval.	D5PM	NA	NA	NA	NA
Demographics						
Behavior Variables, coded by video observation	**Variable Definition**	**Variable Code**	**State Event**	**Point Event**	**Indicator of Instability**	**Indicator of Stability**
Gender	M-Male, F-Female	Sx	NA	NA	NA	NA
Race	AA-African American, W-White non-Hispanic, H-Hispanic	R	NA	NA	NA	NA

Variable List						
Qualitative Variables						
Behavior Variables, coded by video observation	**Variable Definition**	**Variable Code**	**State Event**	**Point Event**	**Indicator of Instability**	**Indicator of Stability**
BW	BW recorded in grams.	BW	NA	NA	NA	NA
Gestational Age	Gestational age recorded by obstetrical dating.	GA	NA	NA	NA	NA
Quantitative Physiological, Longitudinal Variables						
Abdominal Temperature (ABT)	ABT is measured with a skin temperature probe placed on the abdominal surface of the infant.	ABT	x		<36.5C (hypothermia), >37.0C (hyperthermia)	
Foot Temperature (FT)	FT is a peripheral skin temperature measured with a skin temperature probed placed on the sole of the foot.	FT	x		NA	NA
Central-Peripheral Temperature Difference (CPTd)	Thermal gradient between abdomen and foot, ABT-FT=CPTd.	CPTd	x		<0C, >2C	0-2C
Heart Rate (HR)	Beat to beat HR as measured by GE Cardiopulmonary monitor every minute.	HR	x		tachycardia (>200 bpm), bradycardia (<100 bpm), <25% or >75% percentile of daily HR range	inner 50% percentile of daily HR range

Variable List						
Qualitative Variables						
Behavior Variables, coded by video observation	**Variable Definition**	**Variable Code**	**State Event**	**Point Event**	**Indicator of Instability**	**Indicator of Stability**
Respiratory Rate (RR)	RR as measured by the GE Cardiopulmonary monitor every 10 seconds.	RR	x		tachypnea (>60 RR per minute), slow (< 20 RR per minute), <25% or >75% percentile of daily RR	inner 50% percentile of daily RR range

TABLE 5.2 DEMOGRAPHICS

Infant	**GA**	**BW (grams)**	**Gender**	**Race**	**Observation**	**Shift**	**DOL**	**Respiratory Support**	**Feeding**
1	27 5/7	880	F	AA	1	PM	1	Vent	N
					2	PM	2	Vent	N
					3	PM	3	CPAP	N
					4	AM	4	CPAP	N
					5	AM	5	CPAP	N
2	25 3/7	950	M	AA	6	AM	4	CPAP	Y
3	27 1/7	660	F	His	7	AM	1	Vent	N
					8	AM	2	Vent	N
					9	AM	3	Vent	N
4	27 3/7	1040	M	AA	10	PM	4	None	Y
					11	PM	5	None	Y
5	27 4/7	820	F	AA	12	AM	4	Vent	Y
6	27 0/7	940	F	W	13	PM	3	CPAP	N
					14	PM	5	CPAP	N
7	27 4/7	1050	F	AA	15	AM	1	CPAP	N
					16	PM	2	CPAP	N
					17	AM	3	CPAP	Y
					18	PM	4	CPAP	Y
8	28 3/7	1050	F	AA	19	PM	1	CPAP	N
					20	PM	2	CPAP	N

GA: gestational age; F: female; M: male, AA: African American; His: Hispanic; W: White; AM: day shift; PM night shift; Vent: ventilator; CPAP: continuous positive airway pressure; Y: yes, N: no

TABLE 5.3 PERCENTAGE OF STABLE AND STRESS AUTONOMIC, MOTOR, AND STATE BEHAVIORS ACROSS AND WITHIN INTERVALS

		% of Total Behaviors Across the Observation			% Subsystem Behavior Within Interval A			% Subsystem Behavior Within Interval B			% Subsystem Behavior Within Interval C		
		Interval A	Interval B	Interval C	Autonomic	Motor	State	Autonomic	Motor	State	Autonomic	Motor	State
OBS 1	Stable	43%	39%	18%	0%	89%	11%	0%	71%	29%	0%	0%	100%
	Stress	43%	34%	23%	41%	58%	1%	31%	61%	8%	55%	45%	0%
OBS 2	Stable	48%	33%	18%	25%	69%	6%	0%	100%	0%	0%	50%	50%
	Stress	41%	36%	24%	47%	53%	0%	29%	71%	0%	74%	26%	0%
OBS 3	Stable	41%	50%	8%	0%	85%	15%	0%	90%	10%	0%	83%	17%
	Stress	38%	53%	8%	45%	55%	0%	27%	72%	1%	63%	35%	2%
OBS 4	Stable	15%	62%	23%	8%	92%	0%	2%	85%	13%	22%	56%	22%
	Stress	24%	57%	19%	57%	43%	0%	27%	72%	2%	67%	32%	2%
OBS 5	Stable	47%	47%	5%	0%	94%	6%	2%	92%	6%	0%	67%	33%
	Stress	34%	55%	11%	60%	40%	0%	27%	73%	1%	37%	59%	4%
OBS 6	Stable	26%	59%	15%	0%	93%	7%	0%	88%	12%	0%	81%	19%
	Stress	28%	44%	28%	61%	39%	0%	38%	59%	3%	80%	20%	0%
OBS 7	Stable	37%	57%	7%	9%	50%	41%	3%	71%	26%	0%	25%	75%
	Stress	38%	42%	21%	50%	50%	0%	31%	66%	3%	85%	15%	0%

OBS: infant observation; interval A: before caregiving; interval B: during caregiving; interval C: after caregiving; A: autonomic; M: motor; S: state

		% of Total Behaviors Across the Observation			% Subsystem Behavior Within Interval A			% Subsystem Behavior Within Interval B			% Subsystem Behavior Within Interval C		
		Interval A	Interval B	Interval C	Autonomic	Motor	State	Autonomic	Motor	State	Autonomic	Motor	State
OBS 8	Stable	22%	42%	36%	0%	60%	40%	0%	82%	18%	0%	79%	21%
	Stress	19%	42%	39%	47%	51%	2%	34%	64%	2%	49%	47%	3%
OBS 9	Stable	35%	48%	17%	0%	94%	6%	0%	82%	18%	25%	38%	38%
	Stress	50%	47%	3%	82%	18%	0%	15%	82%	3%	0%	100%	0%
OBS 10	Stable	40%	46%	13%	0%	77%	23%	0%	88%	13%	0%	47%	53%
	Stress	42%	52%	6%	33%	62%	6%	27%	71%	2%	77%	19%	3%
OBS 11	Stable	31%	54%	15%	0%	94%	6%	3%	72%	25%	0%	89%	11%
	Stress	27%	55%	18%	35%	65%	0%	22%	78%	0%	97%	3%	0%
OBS 12	Stable	36%	36%	27%	0%	75%	25%	0%	92%	8%	0%	56%	44%
	Stress	40%	42%	18%	87%	13%	0%	17%	82%	1%	65%	32%	3%
OBS 13	Stable	26%	49%	25%	0%	92%	8%	0%	94%	6%	0%	92%	8%
	Stress	26%	50%	24%	57%	43%	0%	21%	79%	0%	85%	15%	0%
OBS 14	Stable	32%	52%	17%	7%	77%	17%	0%	92%	8%	6%	88%	6%
	Stress	25%	45%	30%	50%	50%	0%	22%	76%	2%	74%	26%	0%
OBS 15	Stable	41%	39%	20%	12%	71%	17%	0%	90%	10%	15%	60%	25%
	Stress	32%	52%	17%	52%	48%	0%	31%	67%	3%	91%	9%	0%
OBS 16	Stable	51%	29%	20%	7%	87%	6%	9%	91%	0%	15%	76%	9%
	Stress	47%	39%	14%	39%	61%	0%	27%	73%	0%	82%	18%	6%

OBS: infant observation; interval A: before caregiving; interval B: during caregiving; interval C: after caregiving; A: autonomic; M: motor; S: state

		% of Total Behaviors Across the Observation			% Subsystem Behavior Within Interval A			% Subsystem Behavior Within Interval B			% Subsystem Behavior Within Interval C		
		Interval A	Interval B	Interval C	Autonomic	Motor	State	Autonomic	Motor	State	Autonomic	Motor	State
OBS 17	Stable	30%	42%	28%	22%	70%	8%	23%	77%	0%	6%	80%	14%
	Stress	39%	52%	9%	50%	44%	6%	28%	72%	0%	93%	7%	0%
OBS 18	Stable	35%	46%	19%	0%	95%	5%	1%	96%	2%	6%	79%	15%
	Stress	36%	39%	25%	25%	74%	1%	19%	80%	1%	49%	51%	0%
OBS 19	Stable	62%	25%	13%	0%	98%	2%	0%	100%	0%	0%	0%	0%
	Stress	47%	46%	7%	8%	92%	0%	12%	88%	0%	27%	73%	0%
OBS 20	Stable	36%	52%	12%	0%	85%	15%	0%	99%	1%	0%	100%	0%
	Stress	39%	53%	8%	25%	75%	0%	16%	84%	0%	42%	58%	0%

OBS: infant observation; interval A: before caregiving; interval B: during caregiving; interval C: after caregiving; A: autonomic; M: motor; S: state

TABLE 5.4 TOTAL STABLE AND STRESS BEHAVIORS ACROSS OBSERVATION AND WITHIN INTERVALS

	Behaviors	**Total Across Observation**	**Before Caregiving**	**During Caregiving**	**After Caregiving**
OBS 1	Stable	44	19	17	8
	Stress	263	113	90	60
	Total	307	132	107	68
OBS 2	Stable	33	16	11	6
	Stress	194	79	69	46
	Total	227	95	80	52
OBS 3	Stable	145	60	73	12
	Stress	543	209	288	46
	Total	688	269	361	58
OBS 4	Stable	78	12	48	18
	Stress	349	83	200	66
	Total	427	95	248	84
OBS 5	Stable	110	52	52	6
	Stress	238	80	131	27
	Total	348	132	183	33
OBS 6	Stable	110	29	65	16
	Stress	472	132	209	131
	Total	582	161	274	147
OBS 7	Stable	60	22	34	4
	Stress	288	108	120	60
	Total	348	130	154	64
OBS 8	Stable	92	20	39	33
	Stress	302	57	127	118
	Stable	394	77	166	151
OBS 9	Stable	46	16	22	8
	Stress	145	72	68	5
	Stable	191	88	90	13
OBS 10	Stable	224	90	104	30
	Stress	489	203	255	31
	Total	713	293	359	61
OBS 11	Stable	59	18	32	9
	Stress	187	51	103	33
	Total	246	69	135	42
OBS12	Stable	33	12	12	9
	Stress	206	82	87	37
	Total	239	94	99	46

OBS: infant observation

	Behaviors	Total across observation	Before Caregiving	During Caregiving	After Caregiving
OBS13	Stable	145	38	71	36
	Stress	299	79	149	71
	Total	444	117	220	107
OBS14	Stable	95	30	49	16
	Stress	193	48	87	58
	Total	288	78	136	74
OBS15	Stable	100	41	39	20
	Stress	139	44	72	23
	Total	239	85	111	43
OBS16	Stable	163	83	47	33
	Stress	242	113	95	34
	Total	405	196	142	67
OBS17	Stable	124	37	52	35
	Stress	164	64	85	15
	Total	288	101	137	50
OBS18	Stable	179	63	82	34
	Stress	406	146	157	103
	Total	585	209	239	137
OBS19	Stable	265	164	66	35
	Stress	407	190	187	30
	Total	672	354	253	65
OBS 20	Stable	164	59	85	20
	Stress	288	112	152	24
	Total	452	171	237	44

OBS: infant observation

TABLE 5.5 TOTAL AND PERCENTAGE OF STABLE AND STRESS AUTONOMIC, MOTOR, AND STATE BEHAVIORS BY INTERVAL

		Interval A					Interval B					Interval C			
	Behaviors	Total	A	M	S		Total	A	M	S		Total	A	M	S
OBS 1	Stable	19	0	17	2		17	0	12	5		8	0	0	8
	Stress	113	46	66	1		90	28	55	7		60	33	27	0
	Stable	14%	0%	89%	11%		16%	0.0%	70.6%	29.4%		12%	0%	0%	100%
	Stress	86%	41%	58%	1%		84%	31.1%	61.1%	7.8%		88%	55%	45%	0%
OBS 2	Stable	16	4	11	1		11	0	11	0		6	0	3	3
	Stress	79	37	42	0		69	20	49	0		46	34	12	0
	Stable	17%	25%	69%	6%		14%	0.0%	100.0%	0.0%		12%	0%	50%	50%
	Stress	83%	47%	53%	0%		86%	29.0%	71.0%	0.0%		88%	74%	26%	0%
OBS 3	Stable	60	0	51	9		73	0	66	7		12	0	10	2
	Stress	209	95	114	0		288	79	206	3		46	29	16	1
	Stable	22%	0%	85%	15%		20%	0.0%	90.4%	9.6%		21%	0%	83%	17%
	Stress	78%	45%	55%	0%		80%	27.4%	71.5%	1.0%		79%	63%	35%	2%
OBS 4	Stable	12	1	11	0		48	1	41	6		18	4	10	4
	Stress	83	47	36	0		200	54	143	3		66	44	21	1
	Stable	13%	8%	92%	0%		19%	2.1%	85.4%	12.5%		21%	22%	56%	22%
	Stress	87%	57%	43%	0%		81%	27.0%	71.5%	1.5%		79%	67%	32%	2%
OBS 5	Stable	52	0	49	3		52	1	48	3		6	0	4	2
	Stress	80	48	32	0		131	35	95	1		27	10	16	1
	Stable	39%	0%	94%	6%		28%	1.9%	92.3%	5.8%		18%	0%	67%	33%
	Stress	61%	60%	40%	0%		72%	26.7%	72.5%	0.8%		82%	37%	59%	4%

OBS: infant observation; interval A: before caregiving; interval B: during caregiving; interval C: after caregiving; A: autonomic; M motor; S: state

		Interval A				Interval B				Interval C			
	Behaviors	Total	A	M	S	Total	A	M	S	Total	A	M	S
OBS 6	Stable	29	0	27	2	65	0	57	8	16	0	13	3
	Stress	132	81	51	0	209	79	124	6	131	105	26	0
	Stable	18%	0%	93%	7%	24%	0.0%	87.7%	12.3%	11%	0%	81%	19%
	Stress	82%	61%	39%	0%	76%	37.8%	59.3%	2.9%	89%	80%	20%	0%
OBS 7	Stable	22	2	11	9	34	1	24	9	4	0	1	3
	Stress	108	54	54	0	120	37	79	4	60	51	9	0
	Stable	17%	9%	50%	41%	22%	2.9%	70.6%	26.5%	6%	0%	25%	75%
	Stress	83%	50%	50%	0%	78%	30.8%	65.8%	3.3%	94%	85%	15%	0%
OBS 8	Stable	20	0	12	8	39	0	32	7	33	0	26	7
	Stress	57	27	29	1	127	43	81	3	118	58	56	4
	Stable	26%	0%	60%	40%	23%	0.0%	82.1%	17.9%	22%	0%	79%	21%
	Stress	74%	47%	51%	2%	77%	33.9%	63.8%	2.4%	78%	49%	47%	3%
OBS 9	Stable	16	0	15	1	22	0	18	4	8	2	3	3
	Stress	72	59	13	0	68	10	56	2	5	0	5	0
	Stable	18%	0%	94%	6%	24%	0.0%	81.8%	18.2%	62%	25%	38%	38%
	Stress	82%	82%	18%	0%	76%	14.7%	82.4%	2.9%	38%	0%	100%	0%
OBS 10	Stable	90	0	69	21	104	0	91	13	30	0	14	16
	Stress	203	66	125	12	255	69	182	4	31	24	6	1
	Stable	31%	0%	77%	23%	29%	0.0%	87.5%	12.5%	49%	0%	47%	53%
	Stress	69%	33%	62%	6%	71%	27.1%	71.4%	1.6%	51%	77%	19%	3%
OBS 11	Stable	18	0	17	1	32	1	23	8	9	0	8	1
	Stress	51	18	33	0	103	23	80	0	33	32	1	0
	Stable	26%	0%	94%	6%	24%	3.1%	71.9%	25.0%	21%	0%	89%	11%
	Stress	74%	35%	65%	0%	76%	22.3%	77.7%	0.0%	79%	97%	3%	0%

OBS: infant observation; interval A: before caregiving; interval B: during caregiving; interval C: after caregiving; A: autonomic; M motor; S: state

		Interval A				Interval B				Interval C			
	Behaviors	Total	A	M	S	Total	A	M	S	Total	A	M	S
OBS12	Stable	12	0	9	3	12	0	11	1	9	0	5	4
	Stress	82	71	11	0	87	15	71	1	37	24	12	1
	Stable	13%	0%	75%	25%	12%	0.0%	91.7%	8.3%	20%	0%	56%	44%
	Stress	87%	87%	13%	0%	88%	17.2%	81.6%	1.1%	80%	65%	32%	3%
OBS13	Stable	38	0	35	3	71	0	67	4	36	0	33	3
	Stress	79	45	34	0	149	32	117	0	71	60	11	0
	Stable	32%	0%	92%	8%	32%	0.0%	94.4%	5.6%	34%	0%	92%	8%
	Stress	68%	57%	43%	0%	68%	21.5%	78.5%	0.0%	66%	85%	15%	0%
OBS14	Stable	30	2	23	5	49	0	45	4	16	1	14	1
	Stress	48	24	24	0	87	19	66	2	58	43	15	0
	Stable	38%	7%	77%	17%	36%	0.0%	91.8%	8.2%	22%	6%	88%	6%
	Stress	62%	50%	50%	0%	64%	21.8%	75.9%	2.3%	78%	74%	26%	0%
OBS15	Stable	41	5	29	7	39	0	35	4	20	3	12	5
	Stress	44	23	21	0	72	22	48	2	23	21	2	0
	Stable	48%	12%	71%	17%	35%	0.0%	89.7%	10.3%	47%	15%	60%	25%
	Stress	52%	52%	48%	0%	65%	30.6%	66.7%	2.8%	53%	91%	9%	0%
OBS16	Stable	83	6	72	5	47	4	43	0	33	5	25	3
	Stress	113	44	69	0	95	26	69	0	34	28	6	2
	Stable	42%	7%	87%	6%	33%	8.5%	91.5%	0.0%	49%	15%	76%	9%
	Stress	58%	39%	61%	0%	67%	27.4%	72.6%	0.0%	51%	82%	18%	6%
OBS17	Stable	37	8	26	3	52	12	40	0	35	2	28	5
	Stress	64	32	28	4	85	24	61	0	15	14	1	0
	Stable	37%	22%	70%	8%	38%	23.1%	76.9%	0.0%	70%	6%	80%	14%
	Stress	63%	50%	44%	6%	62%	28.2%	71.8%	0.0%	30%	93%	7%	0%

OBS: infant observation; interval A: before caregiving; interval B: during caregiving; interval C: after caregiving; A: autonomic; M: motor; S: state

		Interval A				Interval B				Interval C			
	Behaviors	Total	A	M	S	Total	A	M	S	Total	A	M	S
OBS18	Stable	63	0	60	3	82	1	79	2	34	2	27	5
	Stress	146	36	108	2	157	30	125	2	103	50	53	0
	Stable	30%	0%	95%	5%	34%	1.2%	96.3%	2.4%	25%	6%	79%	15%
	Stress	70%	25%	74%	1%	66%	19.1%	79.6%	1.3%	75%	49%	51%	0%
OBS19	Stable	164	0	161	3	66	0	66	0	35	0	0	0
	Stress	190	15	175	0	187	23	164	0	30	8	22	0
	Stable	46%	0%	98%	2%	26%	0.0%	100.0%	0.0%	54%	0%	0%	0%
	Stress	54%	8%	92%	0%	74%	12.3%	87.7%	0.0%	46%	27%	73%	0%
OBS 20	Stable	59	0	50	9	85	0	84	1	20	0	20	0
	Stress	112	28	84	0	152	25	127	0	24	10	14	0
	Stable	35%	0%	85%	15%	36%	0.0%	98.8%	1.2%	45%	0%	100%	0%
	Stress	65%	25%	75%	0%	64%	16.4%	83.6%	0.0%	55%	42%	58%	0%

OBS: infant observation; interval A: before caregiving; interval B: during caregiving; interval C: after caregiving; A: autonomic; M: motor; S: state

TABLE 5.6 DESCRIPTIVE STATISTICS FOR INTERVAL A

Interval A						
HR						
Observation	Mean	Standard Deviation	Range	Minimum	Maximum	Missing HR
1	155	13	35	141	176	0
2	145	2	8	142	150	0
3	150	6	31	135	166	0
4	150	3	11	146	157	0
5	155	9	27	144	171	3
6	143	3	10	139	149	0
7	141	7	27	134	161	0
8	141	2	7	139	146	0
9	139	3	9	134	143	0
10	140	8	29	130	159	0
11	147	11	33	132	165	0
12	158	1	4	156	160	0
13	134	5	18	123	141	0
14	136	4	19	126	145	0
15	127	6	22	120	142	0
16	150	5	22	138	160	0
17	138	5	18	130	148	0
18	143	5	19	133	152	0
19	148	2	9	144	153	0
20	144	2	6	141	147	0
CPTd						
Observation	Mean	Standard Deviation	Range	Minimum	Maximum	Missing HR
1	-0.64	0.1	0.24	-0.74	-0.5	0
2	-0.35	0.01	0.05	-0.4	-0.35	0
3	1.21	0.04	0.18	1.15	1.33	0
4	0.12	0.02	0.1	0.07	0.17	0
5	0.27	0.05	0.14	0.21	0.35	0
6	0.19	0.31	1.03	-0.35	0.68	0
7	0.57	0.07	0.27	0.36	0.63	0

8	1.28	0.04	0.1	1.21	1.31	0
9	1.18	0.14	0.35	1.02	1.37	0
10	0.69	0.12	0.45	0.46	0.91	0
11	0.69	0.13	0.45	0.5	0.95	0
12	-0.2	0.06	0.22	-0.27	-0.05	0
13	1.21	0.1	0.32	1.05	1.37	0
14	1.31	0.19	0.56	1.01	1.57	0
15	0.55	0	0	0.55	0.55	0
16	0.24	0.06	0.18	0.13	0.31	0
17	0.3	0.05	0.2	0.2	0.4	0
18	1.51	0.14	0.51	1.3	1.81	0
19	1.18	0.14	0.44	0.94	1.38	0
20	0.78	0.33	1.29	0.43	1.72	0
ABT						
Observation	Mean	Standard Deviation	Range	Minimum	Maximum	Missing HR
1	35.21	0.01	0.07	35.18	35.25	0
2	35.23	0	0	35.23	35.23	0
3	36.68	0.01	0.05	36.63	36.68	0
4	36.8	0	0	36.8	36.8	0
5	36.28	0.03	0.13	36.2	36.33	0
6	36.27	0.25	1.05	35.69	36.74	0
7	37.21	0.05	0.2	37.06	37.26	0
8	37.04	0.02	0.05	37.01	37.06	0
9	36.85	0	0	36.85	36.85	0
10	37.35	0.03	0.1	37.31	37.41	0
11	36.69	0.07	0.2	36.58	36.78	0
12	34.32	0.07	0.22	34.24	34.46	0
13	36.61	0.11	0.35	36.47	36.82	0
14	36.81	0.1	0.33	36.62	36.95	0
15	36.83	0	0	36.83	36.83	0
16	36.47	0.04	0.1	36.43	36.53	0
17	36.66	0.07	0.2	36.58	36.78	0
18	36.46	0.1	0.38	36.25	36.63	0
19	36.96	0.05	0.15	36.91	37.06	0
20	36.46	0.04	0.15	36.38	36.53	0

TABLE 5.7 DESCRIPTIVE STATISTICS FOR INTERVAL B

Interval B						
HR						
Observation	Mean	Standard Deviation	Range	Minimum	Maximum	Missing HR
1	164	7	35	153	174	0
2	153	7	24	143	167	0
3	156	6	25	146	171	1
4	162	10	32	147	179	0
5	159	12	31	147	178	0
6	145	5	19	138	157	0
7	140	7	28	134	162	1
8	144	4	15	139	154	0
9	156	8	21	145	166	0
10	152	11	41	133	174	1
11	135	3	12	130	142	1
12	156	2	8	152	160	0
13	133	5	18	122	140	0
14	146	11	29	133	162	0
15	131	9	31	119	150	1
16	155	7	22	143	165	0
17	146	10	33	132	165	0
18	152	8	26	139	165	0
19	153	3	12	145	157	2
20	147	3	10	144	154	0
CPTd						
Observation	Mean	Standard Deviation	Range	Minimum	Maximum	Missing HR
1	-0.27	0.17	0.5	-0.55	-0.05	0
2	-0.04	0.7	1.86	-0.67	1.19	0
3	1.2	0.13	0.39	1.02	1.41	0
4	1.17	0.86	2.54	0.02	2.56	0
5	0.66	0.39	1.37	0.12	1.49	0
6	0.77	0.09	0.3	0.65	0.95	0
7	0.39	0.36	1.9	-0.83	1.07	0

8	0.92	0.29	0.94	0.44	1.38	0
9	1.08	0.19	0.68	0.62	1.3	0
10	0.59	0.49	1.83	-0.25	1.58	0
11	0.87	0.31	1.04	0.29	1.33	0
12	0.72	1.14	2.94	-1.07	1.87	0
13	1.31	0.05	0.15	1.27	1.42	0
14	0.76	0.11	0.33	0.63	0.96	0
15	0.69	0.66	2.76	-1.52	1.24	0
16	-0.7	0.75	2.9	-2.52	0.38	0
17	0.45	0.16	0.46	0.2	0.66	0
18	1.16	0.79	2.66	0.15	2.81	8
19	0.75	0.29	1.1	0.2	1.3	0
20	1.3	0.42	1.51	0.48	1.99	0
ABT						
Observation	Mean	Standard Deviation	Range	Minimum	Maximum	Missing HR
1	35.15	0.12	0.32	34.96	35.28	0
2	35.14	0.6	1.87	34.2	36.07	0
3	36.36	0.14	0.45	36.15	36.6	0
4	36.4	0.08	0.78	36.02	36.8	0
5	35.49	0.47	1.46	34.69	36.15	0
6	36.73	0.09	0.28	36.59	36.87	0
7	36.48	0.39	1.88	35.3	37.18	0
8	36.91	0.2	1.04	36.02	37.06	0
9	36.64	0.23	0.78	36.02	36.8	0
10	36.41	0.53	1.99	35.3	37.29	0
11	36.62	0.26	1.06	35.87	36.93	0
12	35.16	1.04	2.48	33.56	36.04	0
13	36.44	0.1	0.33	36.24	36.57	0
14	37.05	0.06	0.2	36.95	37.15	0
15	36.39	0.7	2.95	33.88	36.83	0
16	36.34	0.18	0.6	36.05	36.65	0
17	36.7	0.09	0.25	36.53	36.78	0
18	35.54	0.92	2.54	33.91	36.45	0
19	36.41	0.32	1.01	35.9	36.91	0
20	36.36	0.06	0.23	36.2	36.43	0

TABLE 5.8 DESCRIPTIVE STATISTICS FOR INTERVAL C

Interval C						
HR						
Observation	Mean	Standard Deviation	Range	Minimum	Maximum	Missing HR
1	170	6	18	158	176	0
2	147	2	7	144	151	0
3	157	6	22	152	174	0
4	156	9	32	146	178	0
5	154	7	21	147	168	1
6	151	6	20	144	164	0
7	138	7	26	131	157	1
8	152	9	28	142	170	0
9	137	5	12	132	144	0
10	146	15	70	101	171	0
11	136	5	17	131	148	0
12	154	0.4	4	152	156	0
13	134	5	18	123	141	0
14	143	13	38	120	158	0
15	131	6	16	124	140	0
16	144	7	22	137	159	1
17	143	13	42	132	174	0
18	142	9	28	133	161	1
19	151	3	12	146	158	1
20	147	3	12	142	154	0
CPTd						
Observation	Mean	Standard Deviation	Range	Minimum	Maximum	Missing HR
1	-0.35	0.01	0.1	-0.37	-0.27	0
2	0.59	0.3	0.89	0.15	1.04	0
3	1.39	0.15	0.57	1.1	1.67	0
4	1.34	0.23	0.64	0.99	1.63	0
5	1.15	0.15	0.52	0.77	1.29	0
6	0.36	0.14	0.47	0.05	0.52	0
7	0.38	0.15	0.46	0.15	0.61	0
8	0.63	0.06	0.2	0.56	0.76	0

9	1.16	0.13	0.32	0.98	1.3	0
10	1.09	0.29	0.83	0.8	1.63	0
11	1.08	0.2	0.57	0.71	1.28	0
12	0.11	0.34	1.22	1.56	0	0.11
13	1.13	0.04	0.15	1.07	1.22	0
14	0.54	0.05	0.15	0.48	0.63	0
15	0.48	0.1	0.3	0.33	0.63	0
16	-2.3	0.59	1.95	-3.17	-1.22	0
17	0.34	0.16	0.48	0.15	0.63	0
18	1.03	0.11	0.39	0.84	1.23	0
19	0.45	0.2	0.58	0.2	0.78	0
20	0.88	0.25	0.79	0.6	1.39	0
ABT						
Observation	Mean	Standard Deviation	Range	Minimum	Maximum	Missing HR
1	35.21	0	0	35.21	35.21	0
2	36.18	0.17	0.57	35.68	36.25	0
3	36.67	0.14	0.4	36.43	36.83	0
4	36.04	0.12	0.37	35.83	36.2	0
5	35.38	0.16	0.45	35.18	35.63	0
6	36.64	0.24	0.7	36.17	36.87	0
7	36.66	0.06	0.23	36.5	36.73	0
8	37.1	0.05	0.15	37.01	37.16	0
9	36.84	0.05	0.1	36.78	36.88	0
10	36.29	0.16	0.85	35.63	36.48	0
11	36.91	0.02	0.05	36.88	36.93	0
12	36.2	0.01	0.15	36.07	36.22	0
13	36.2	0.04	0.13	36.14	36.27	0
14	37.24	0.05	0.15	37.15	37.3	0
15	36.33	0.01	0.05	36.28	36.33	0
16	34.55	0.53	1.74	33.74	35.48	0
17	36.54	0.02	0.05	36.53	36.58	0
18	35.9	0.02	0.32	35.7	36.02	0
19	36.33	0.06	0.2	36.2	36.4	0
20	36.43	0.04	0.13	36.4	36.53	0

TABLE 5.9 MODEL COMPARISONS

		Interval A	Interval B	Interval C
OBS 1	Model 1	U	U	U
	Model 2	U	U	M
OBS 2	Model 1	U	U	M
	Model 2	U	U	M
OBS 3	Model 1	U	U	U
	Model 2	S	M	M
OBS 4	Model 1	U	U	S
	Model 2	S	M	M
OBS 5	Model 1	M	U	S
	Model 2	M	M	M
OBS 6	Model 1	U	U	U
	Model 2	M	M	M
OBS 7	Model 1	U	U	U
	Model 2	S	M	M
OBS 8	Model 1	U	U	U
	Model 2	S	M	M
OBS 9	Model 1	U	U	M
	Model 2	S	S	S
OBS 10	Model 1	M	U	M
	Model 2	S	M	M
OBS 11	Model 1	M	U	U
	Model 2	S	S	S
OBS 12	Model 1	U	U	U
	Model 2	U	M	M
OBS 13	Model 1	M	M	M
	Model 2	M	M	M
OBS 14	Model 1	M	M	M
	Model 2	M	M	M
OBS 15	Model 1	M	M	M
	Model 2	M	M	U
OBS 16	Model 1	M	M	M
	Model 2	S	M	U
OBS 17	Model 1	M	M	M
	Model 2	S	S	S
OBS 18	Model 1	M	M	M
	Model 2	M	M	M
OBS 19	Model 1	M	U	M
	Model 2	S	S	M
OBS 20	Model 1	M	M	M
	Model 2	M	M	M

S= Stable U = Instable M =Mixed

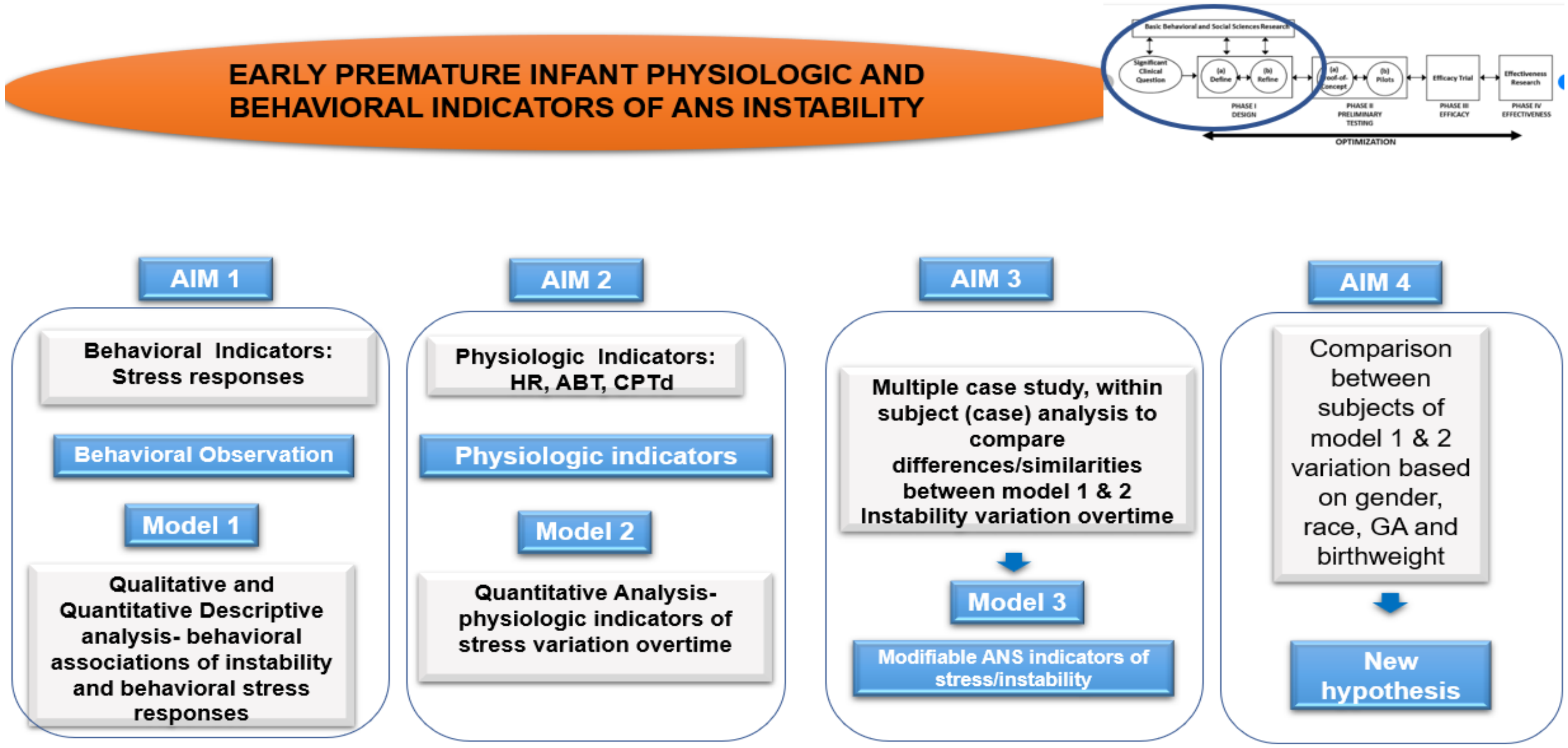

FIGURE 5.1 RESEARCH AIMS AND MODELS

HR: heart rate, RR: respiratory rate; ABT: abdominal temperature; FT: foot temperature: CPTd: central- peripheral temperature difference; GA: Gestational Age, PCA: Post Conceptual age

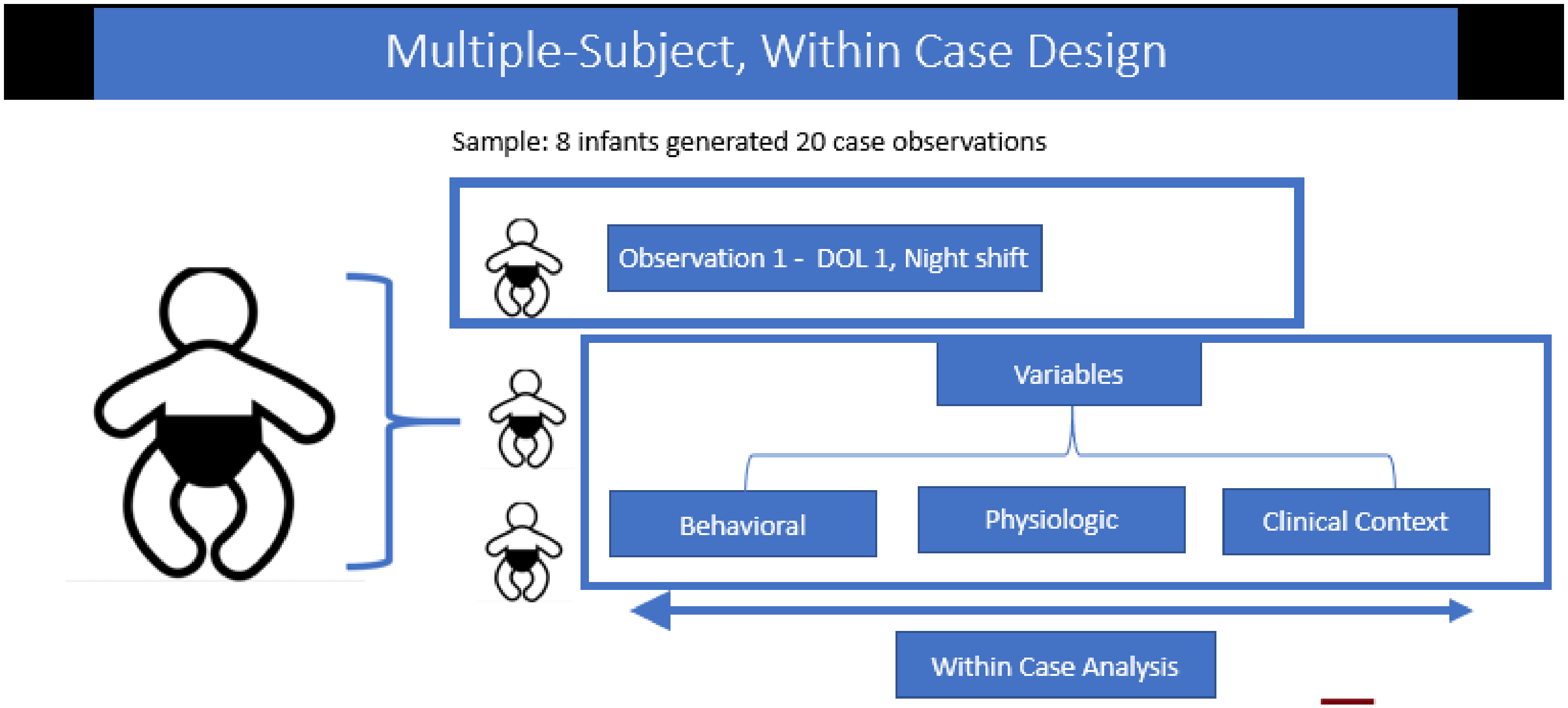

FIGURE 5.2 MULTIPLE SUBJECT WITHIN-CASE DESIGN

DOL: Day of life

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APPENDIX A

COMBINED BEHAVIORAL AND PHYSIOLOGIC MEASURES OF ALL CASES

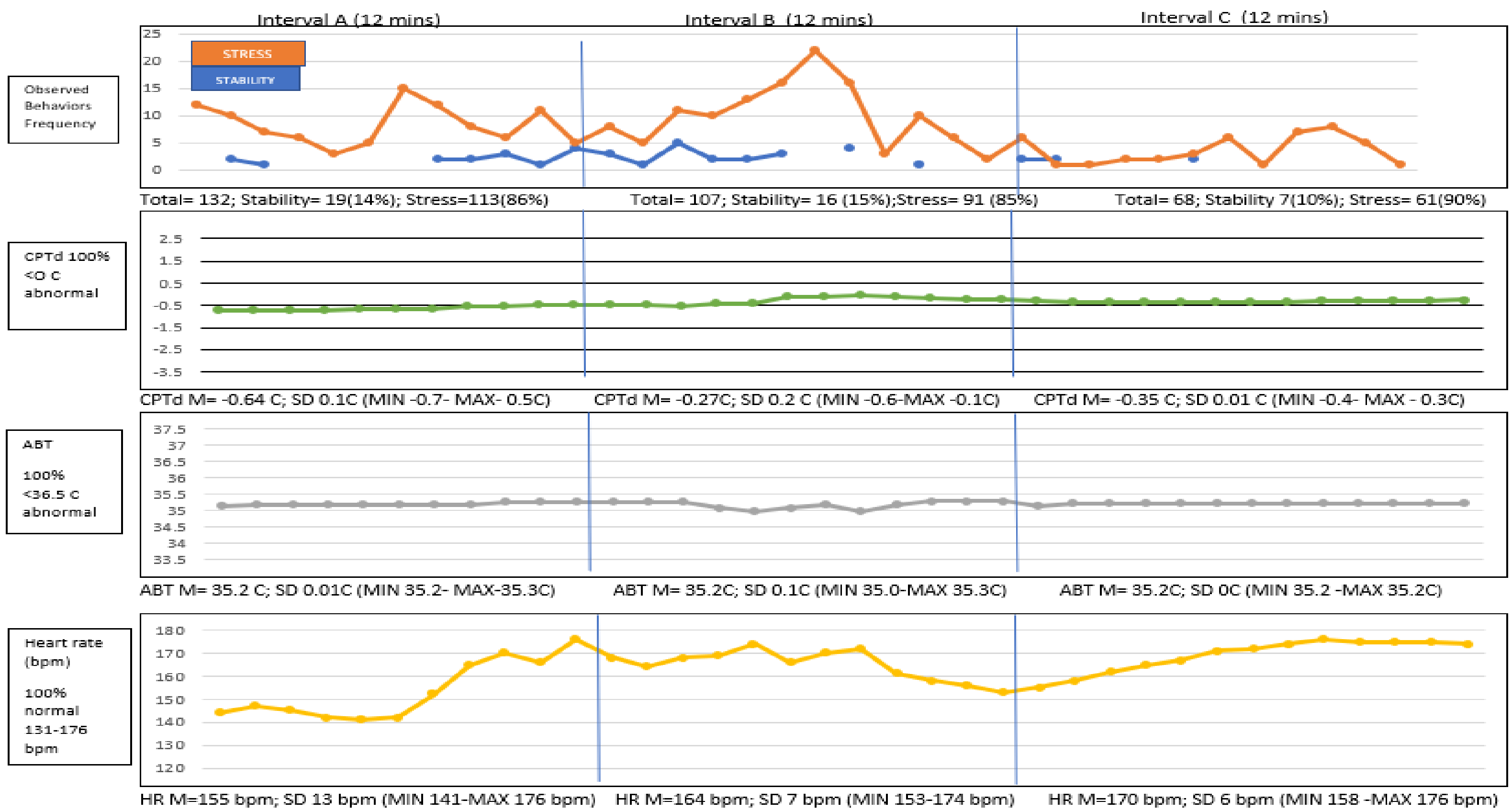

FIGURE A.1 OBSERVATION 1 COMBINED BEHAVIORAL AND PHYSIOLOGIC MEASURES

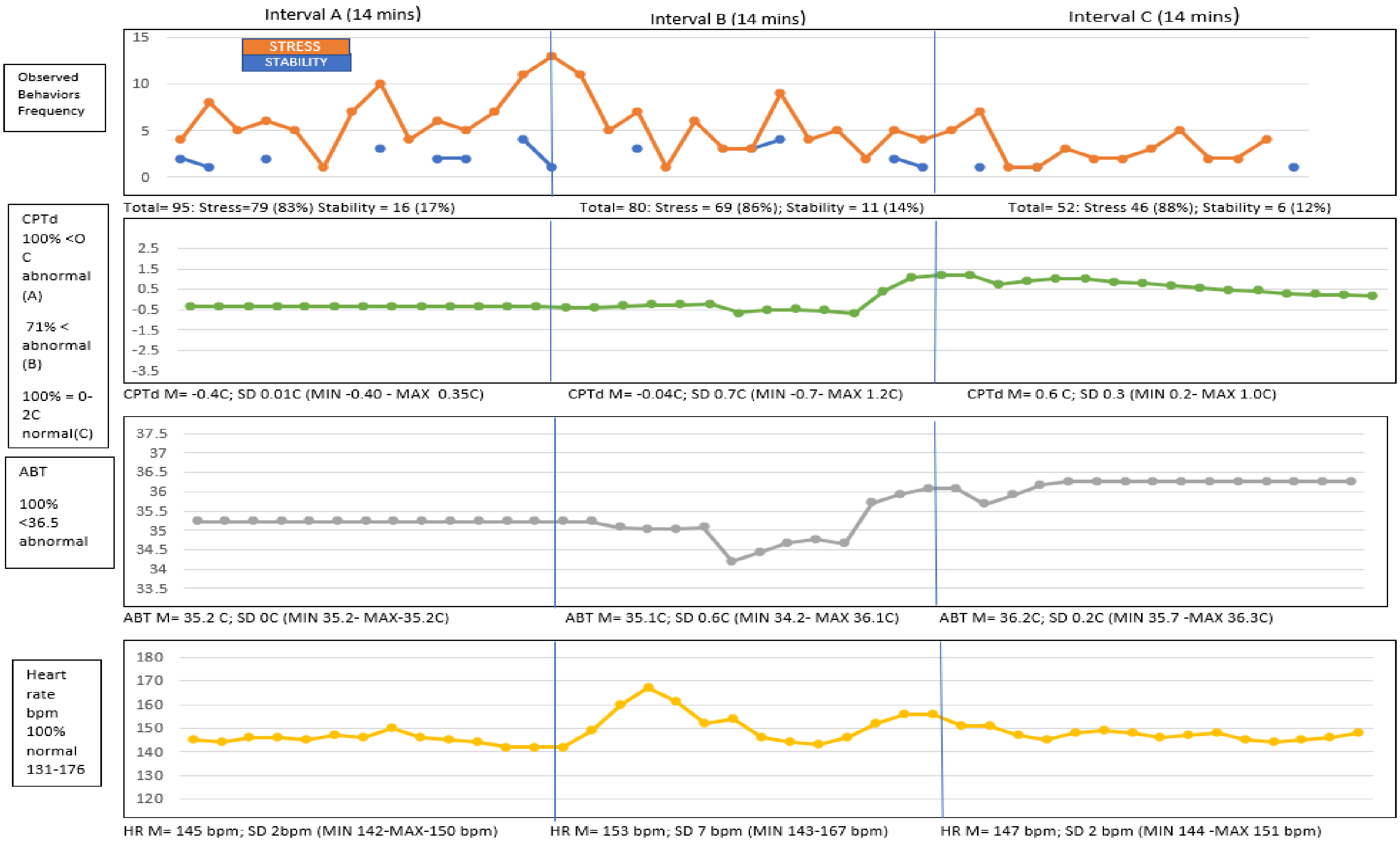

FIGURE A.2 OBSERVATION 2 COMBINED BEHAVIORAL AND PHYSIOLOGIC MEASURES

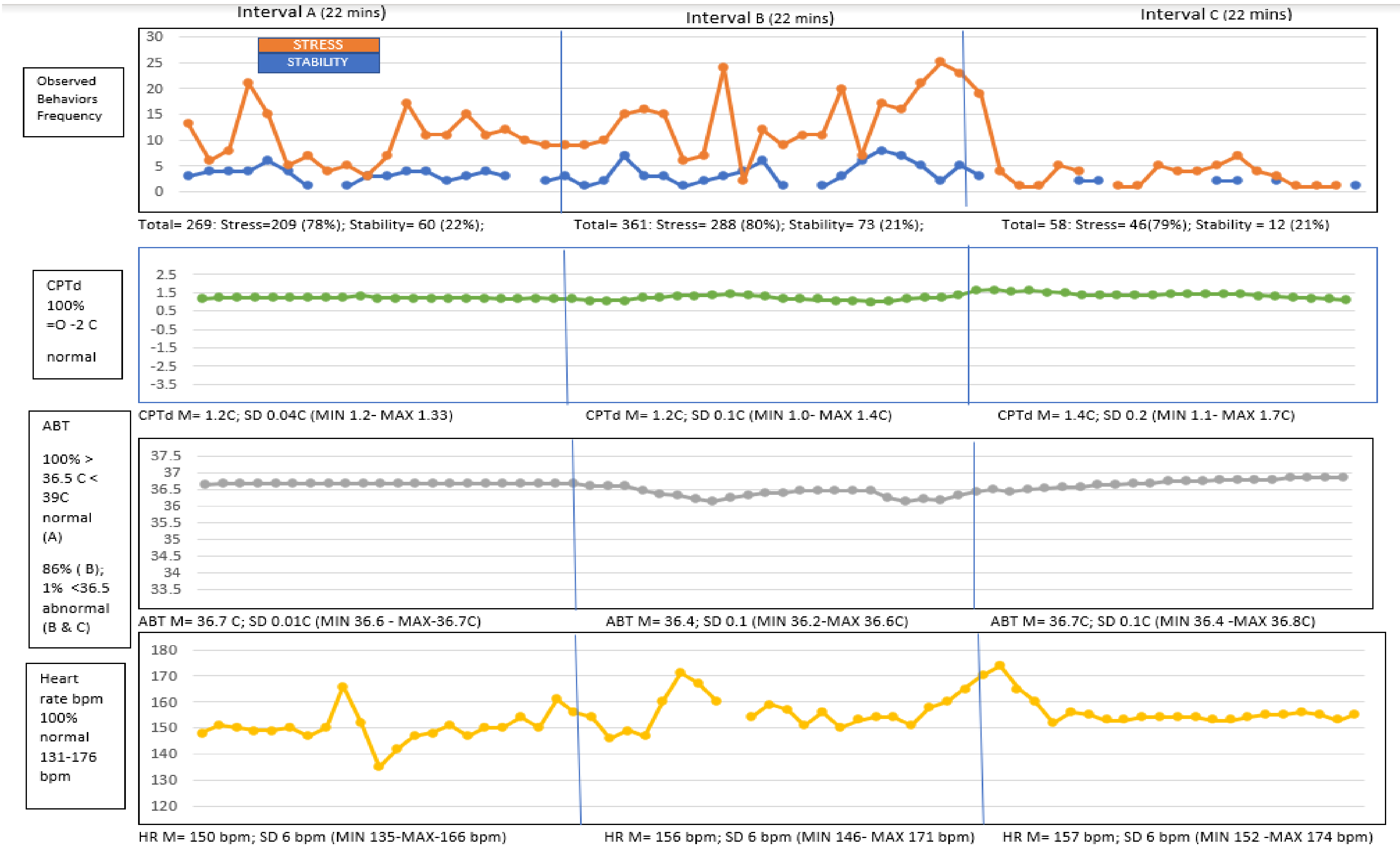

FIGURE A.3 OBSERVATION 3 COMBINED BEHAVIORAL AND PHYSIOLOGIC MEASURES

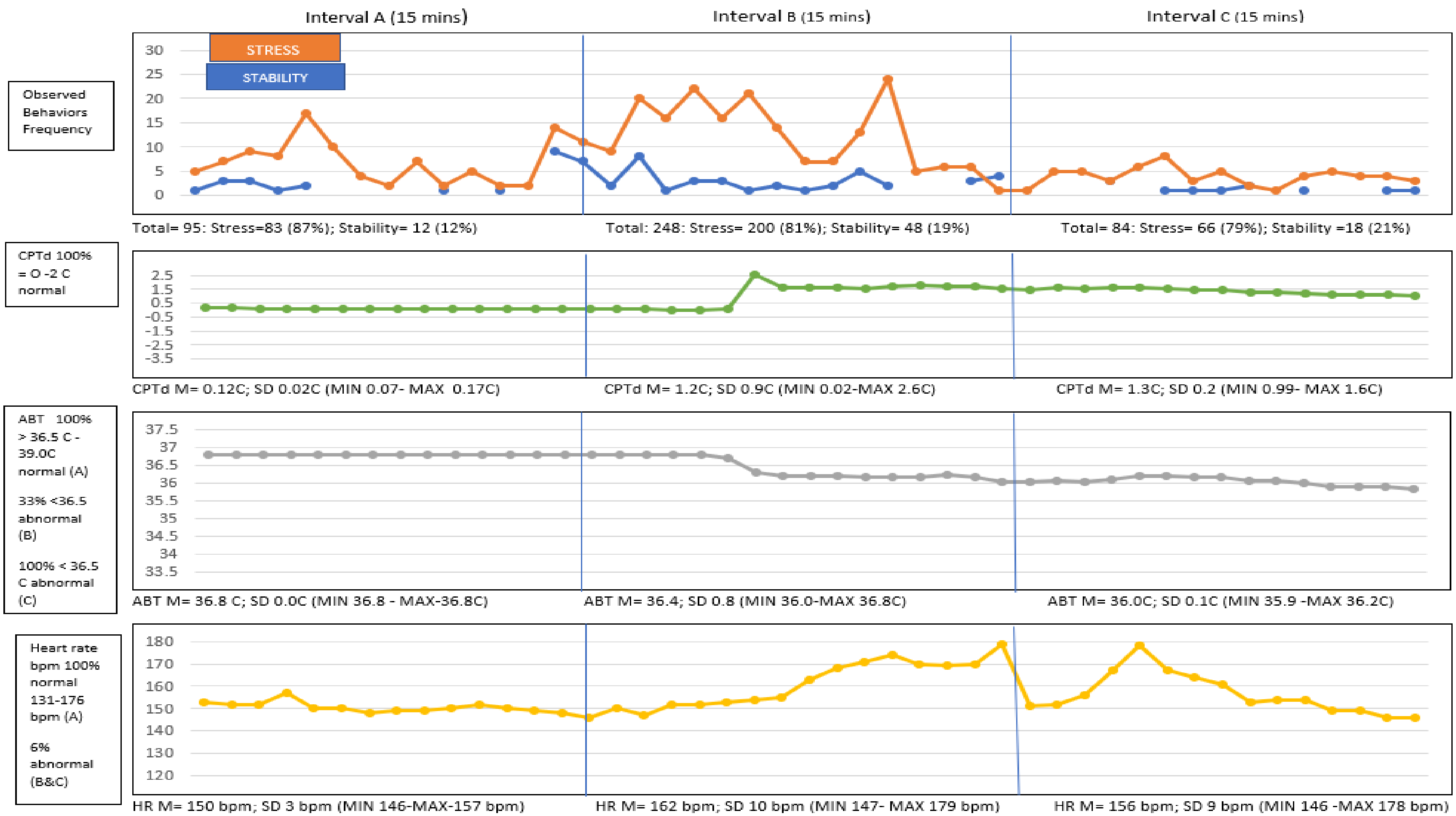

FIGURE A.4 OBSERVATION 4 COMBINED BEHAVIORAL AND PHYSIOLOGIC MEASURES

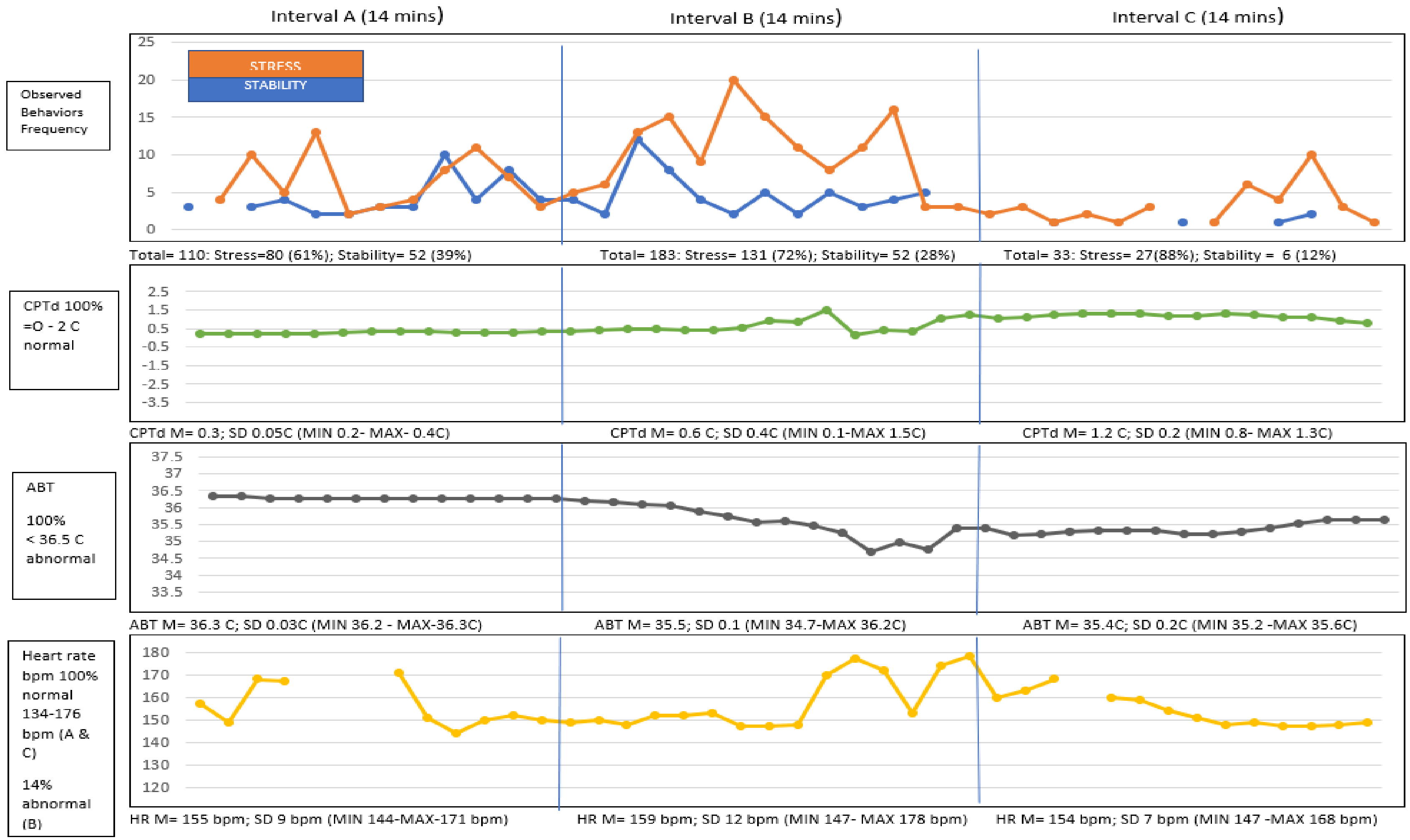

FIGURE A.5 OBSERVATION 5 COMBINED BEHAVIORAL AND PHYSIOLOGIC MEASURES

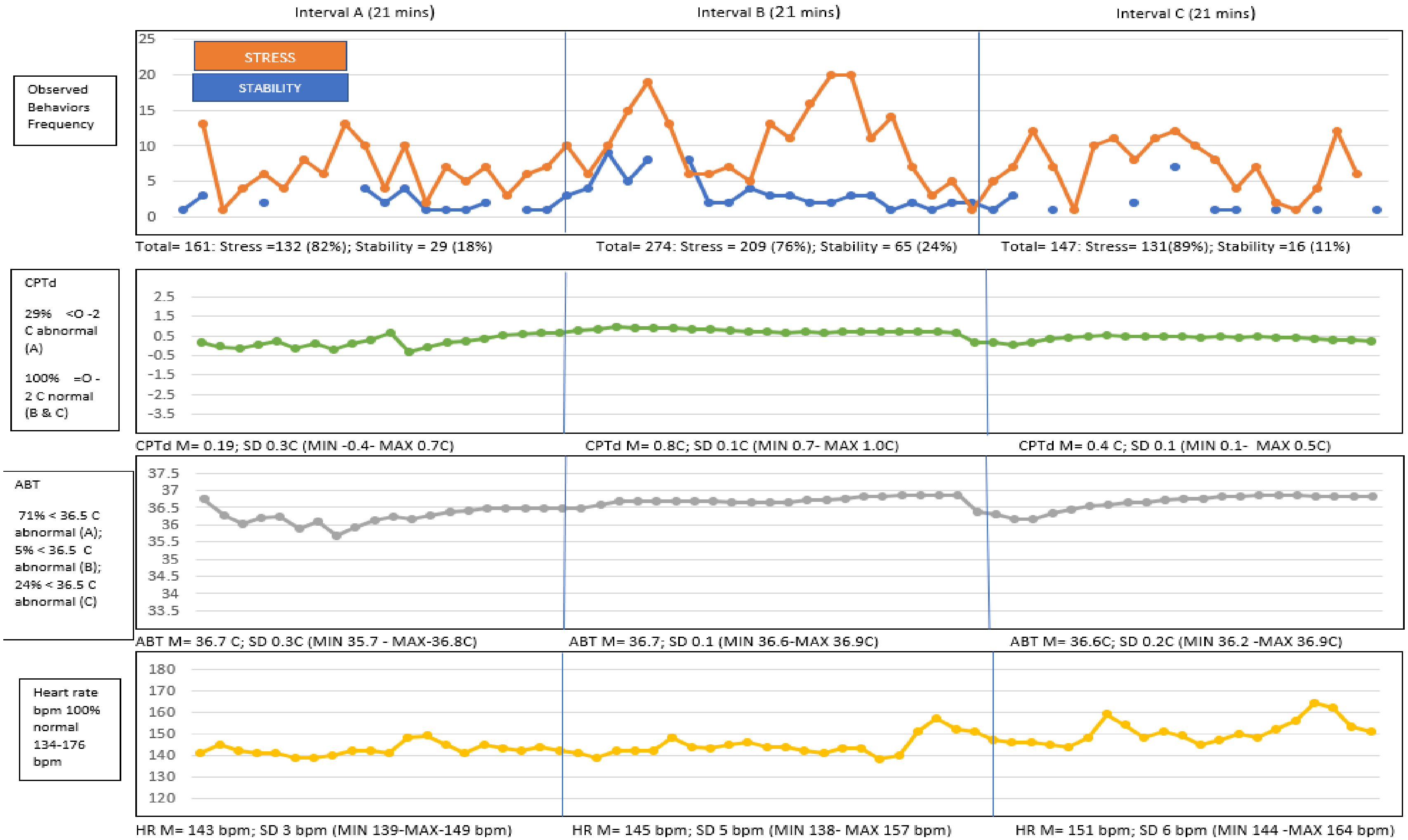

FIGURE A.6 OBSERVATION 6 COMBINED BEHAVIORAL AND PHYSIOLOGIC MEASURES

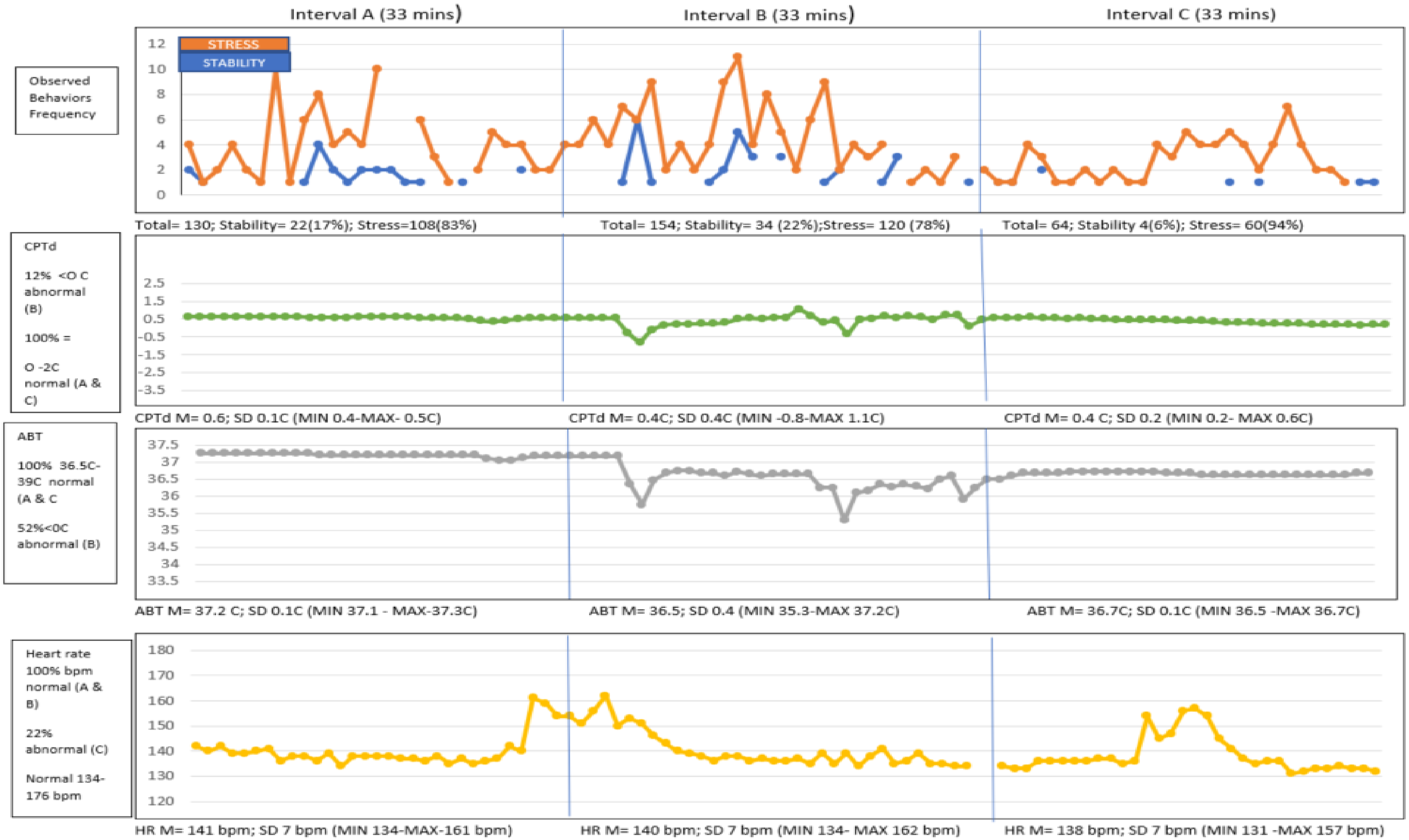

FIGURE A.7 OBSERVATION 7 COMBINED BEHAVIORAL AND PHYSIOLOGIC MEASURES

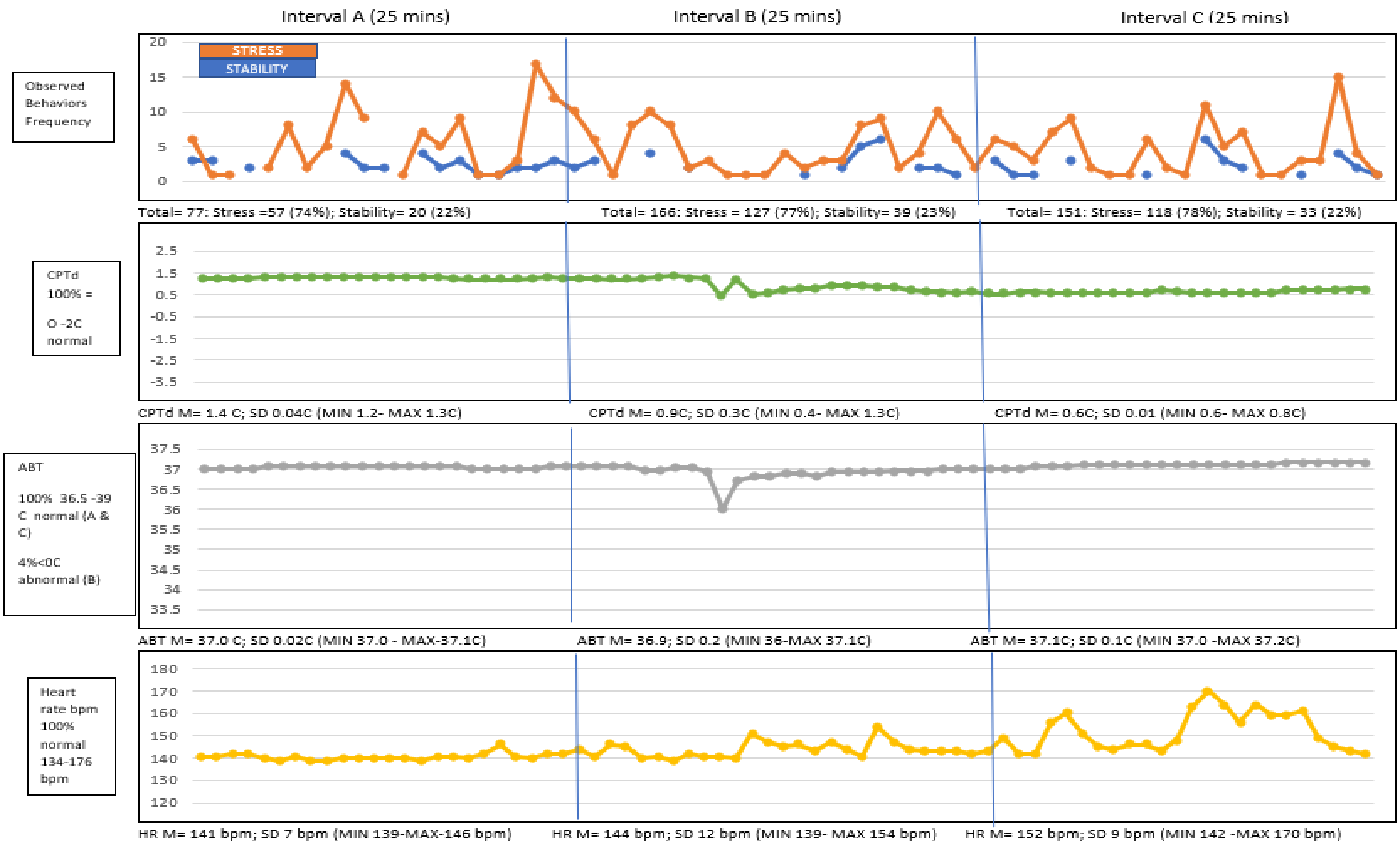

FIGURE A.8 OBSERVATION 8 COMBINED BEHAVIORAL AND PHYSIOLOGIC MEASURES

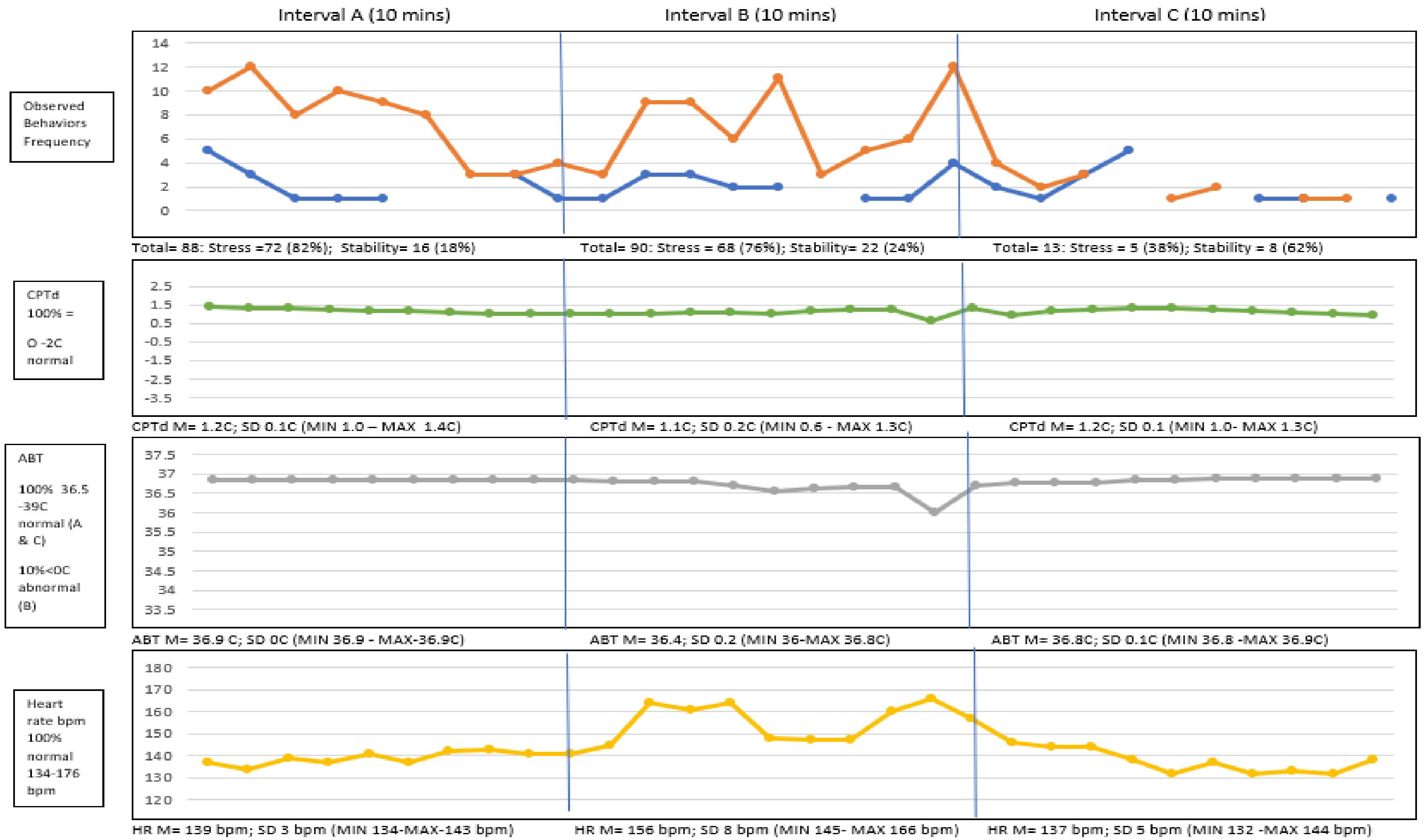

FIGURE A.9 OBSERVATION 9 COMBINED BEHAVIORAL AND PHYSIOLOGIC MEASURES

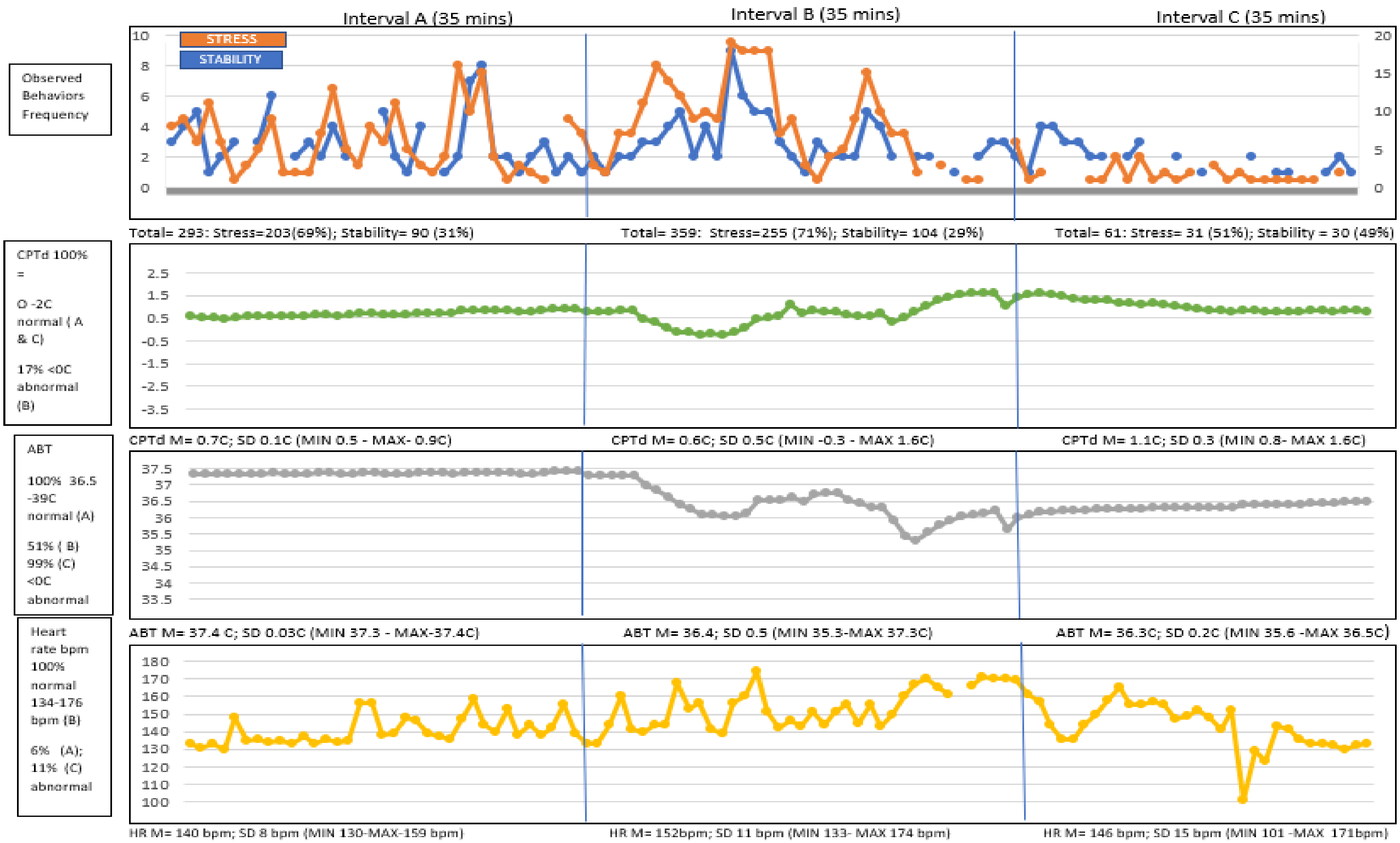

FIGURE A.10 OBSERVATION 10 COMBINED BEHAVIORAL AND PHYSIOLOGIC MEASURES

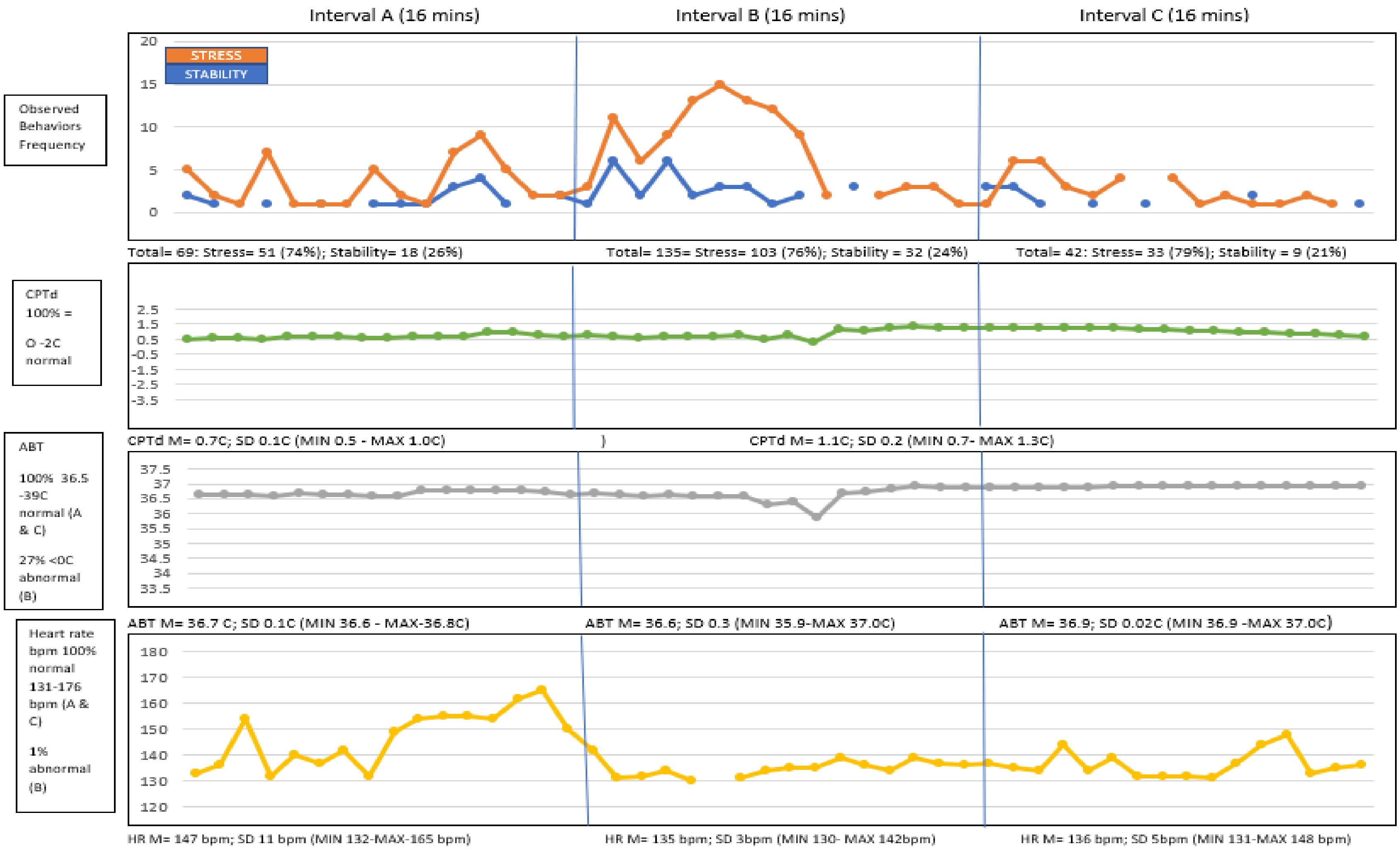

FIGURE A.11 OBSERVATION 11 COMBINED BEHAVIORAL AND PHYSIOLOGIC MEASURES

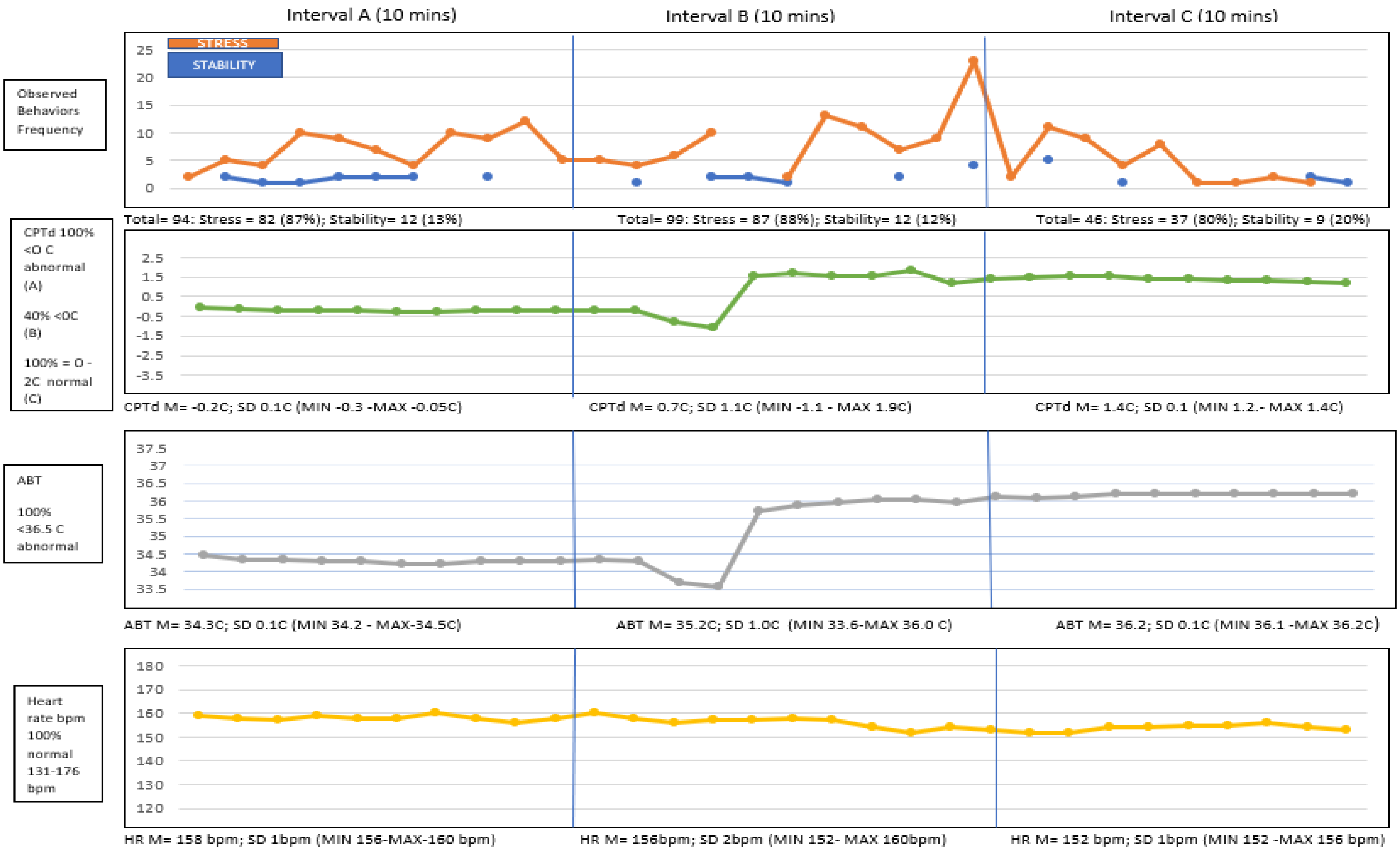

FIGURE A.12 OBSERVATION 12 COMBINED BEHAVIORAL AND PHYSIOLOGIC MEASURES

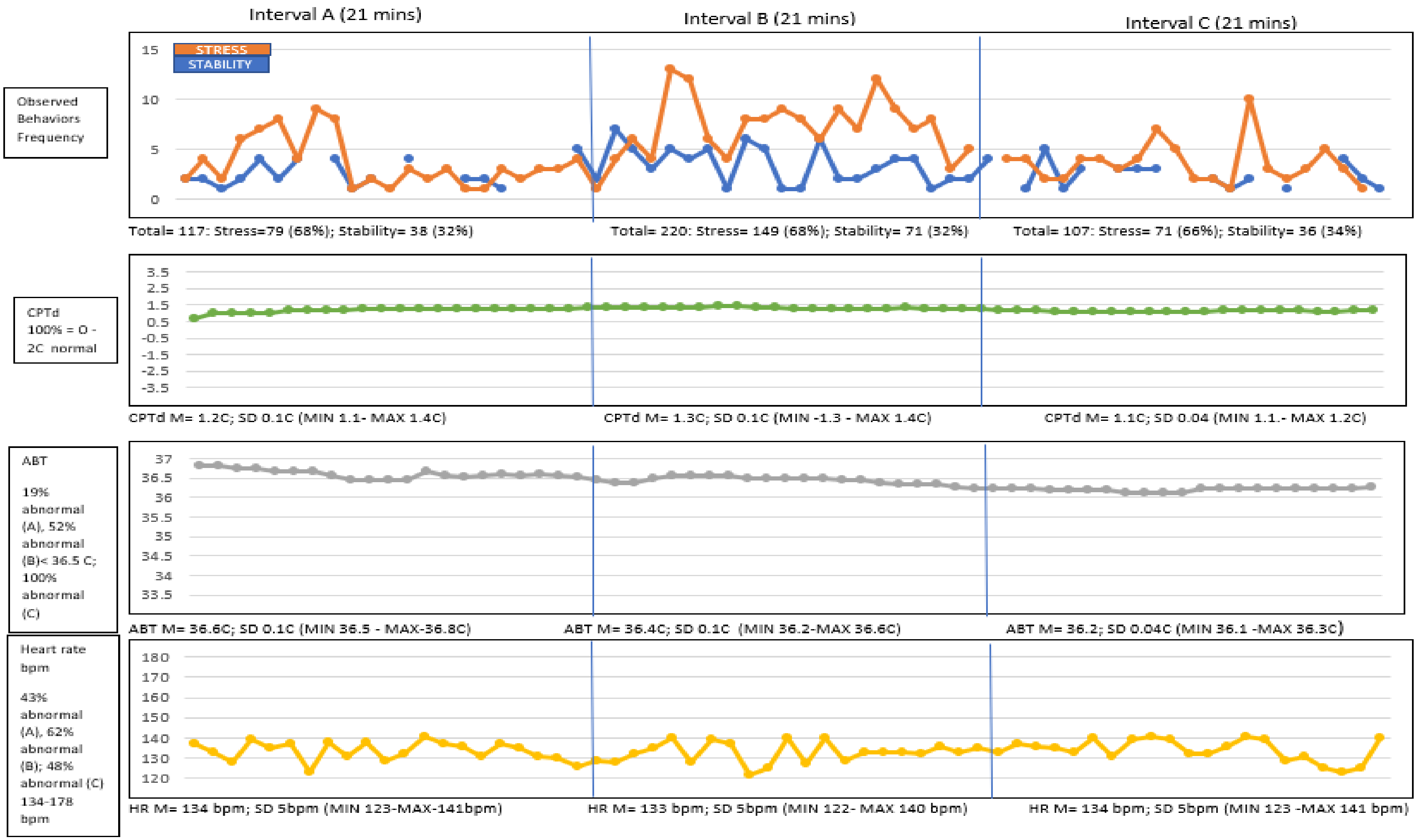

FIGURE A.13 OBSERVATION 13 COMBINED BEHAVIORAL AND PHYSIOLOGIC MEASURES

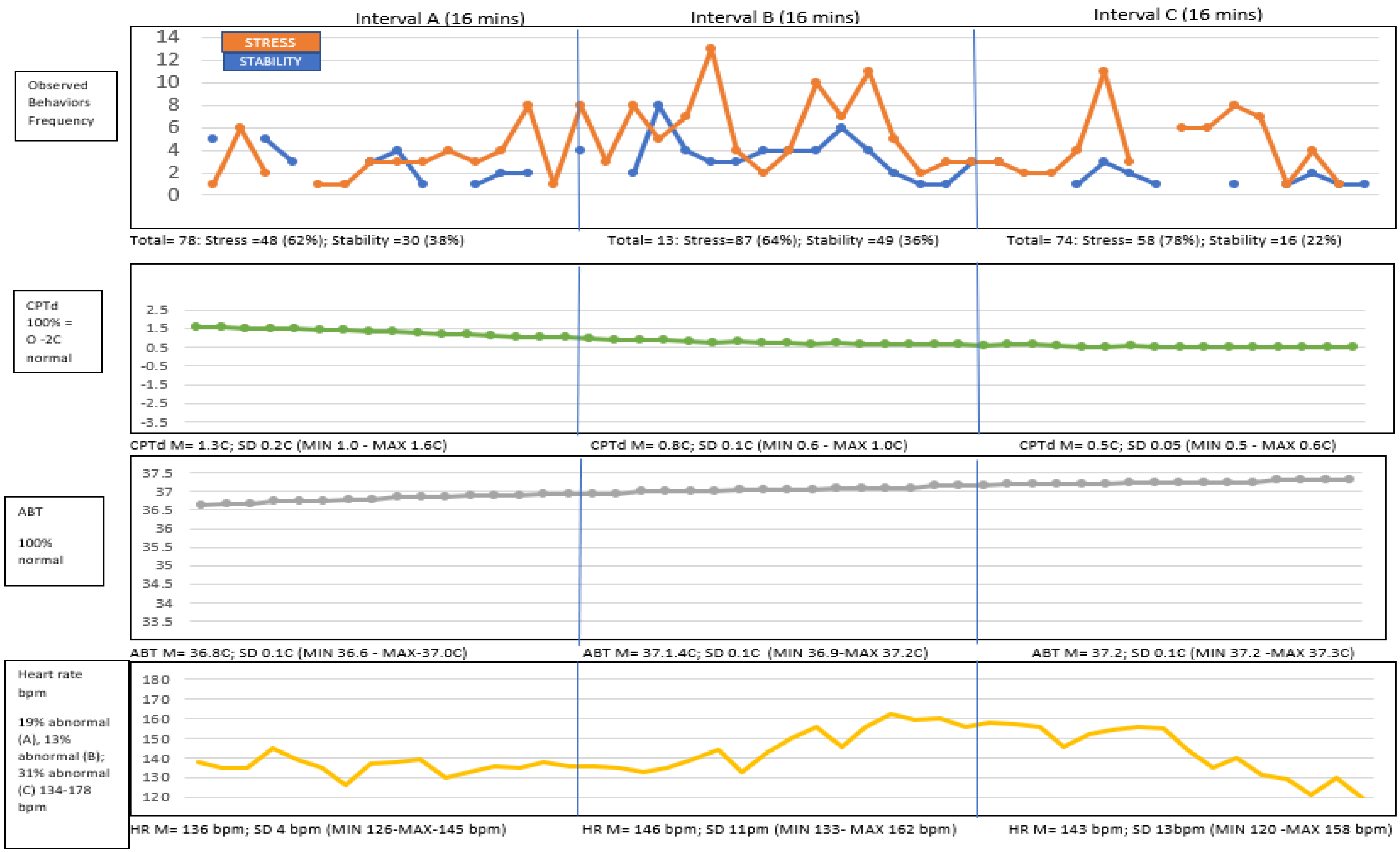

FIGURE A.14 OBSERVATION 14 COMBINED BEHAVIORAL AND PHYSIOLOGIC MEASURES

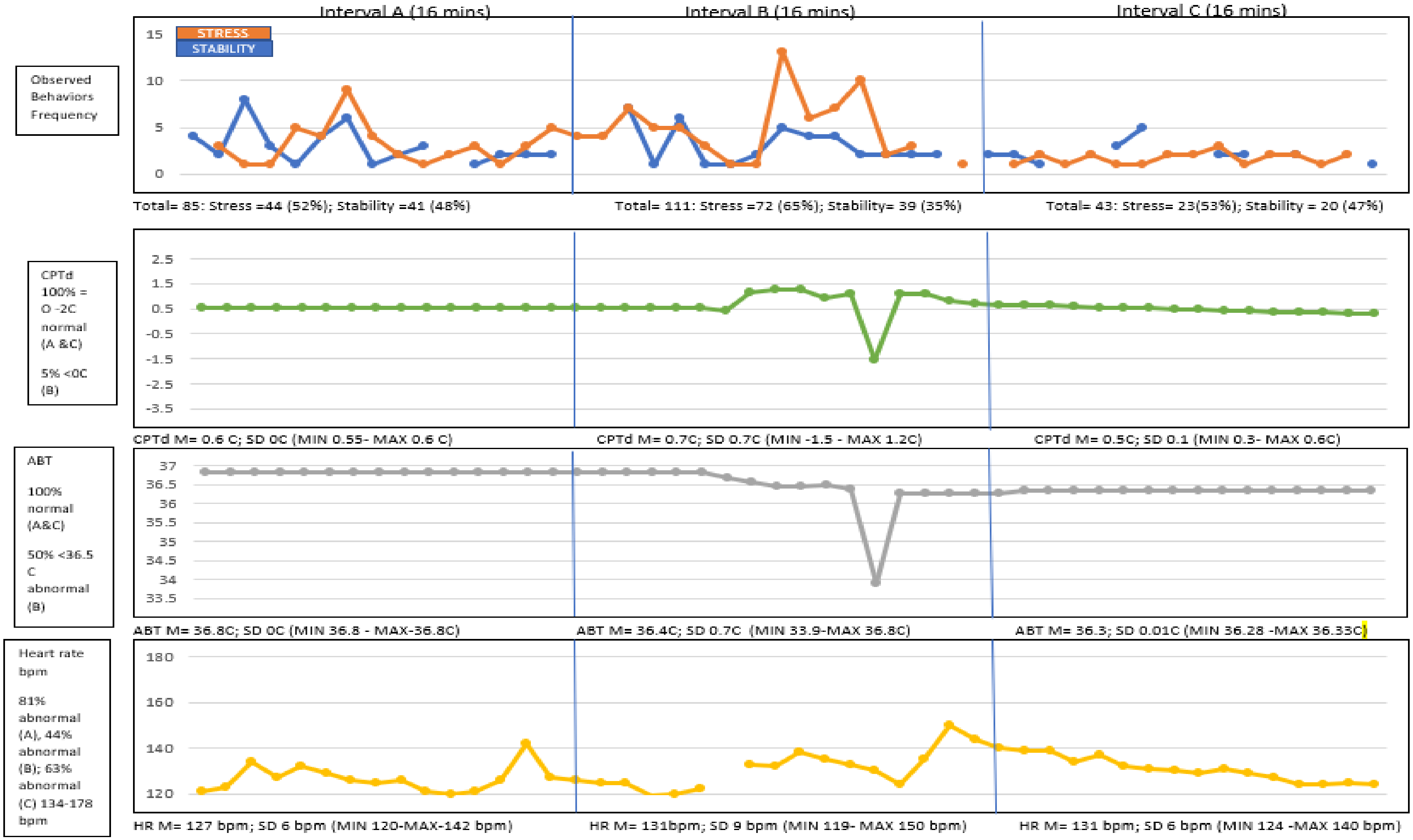

FIGURE A.15 OBSERVATION 15 COMBINED BEHAVIORAL AND PHYSIOLOGIC MEASURES

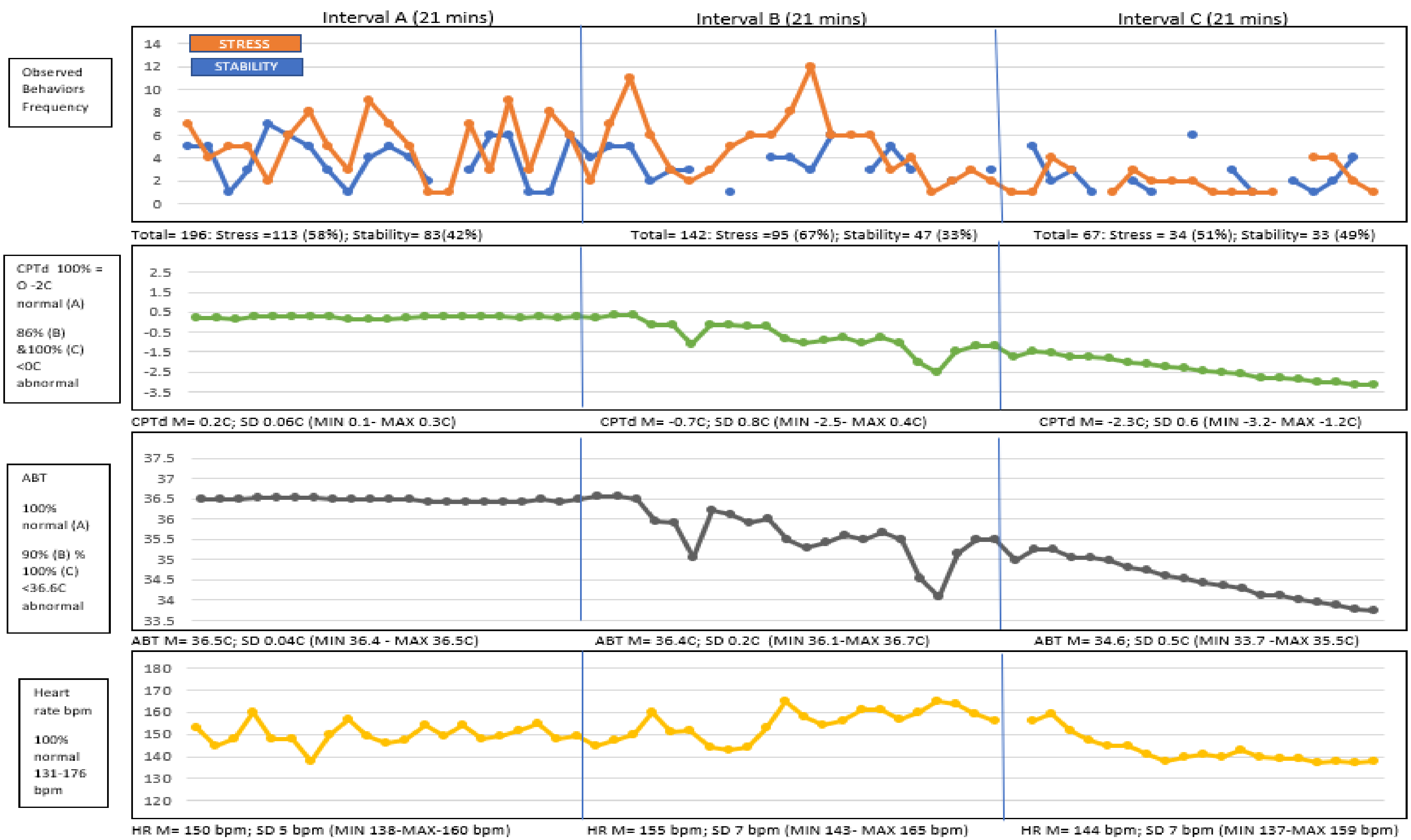

FIGURE A.16 OBSERVATION 16 COMBINED BEHAVIORAL AND PHYSIOLOGIC MEASURES

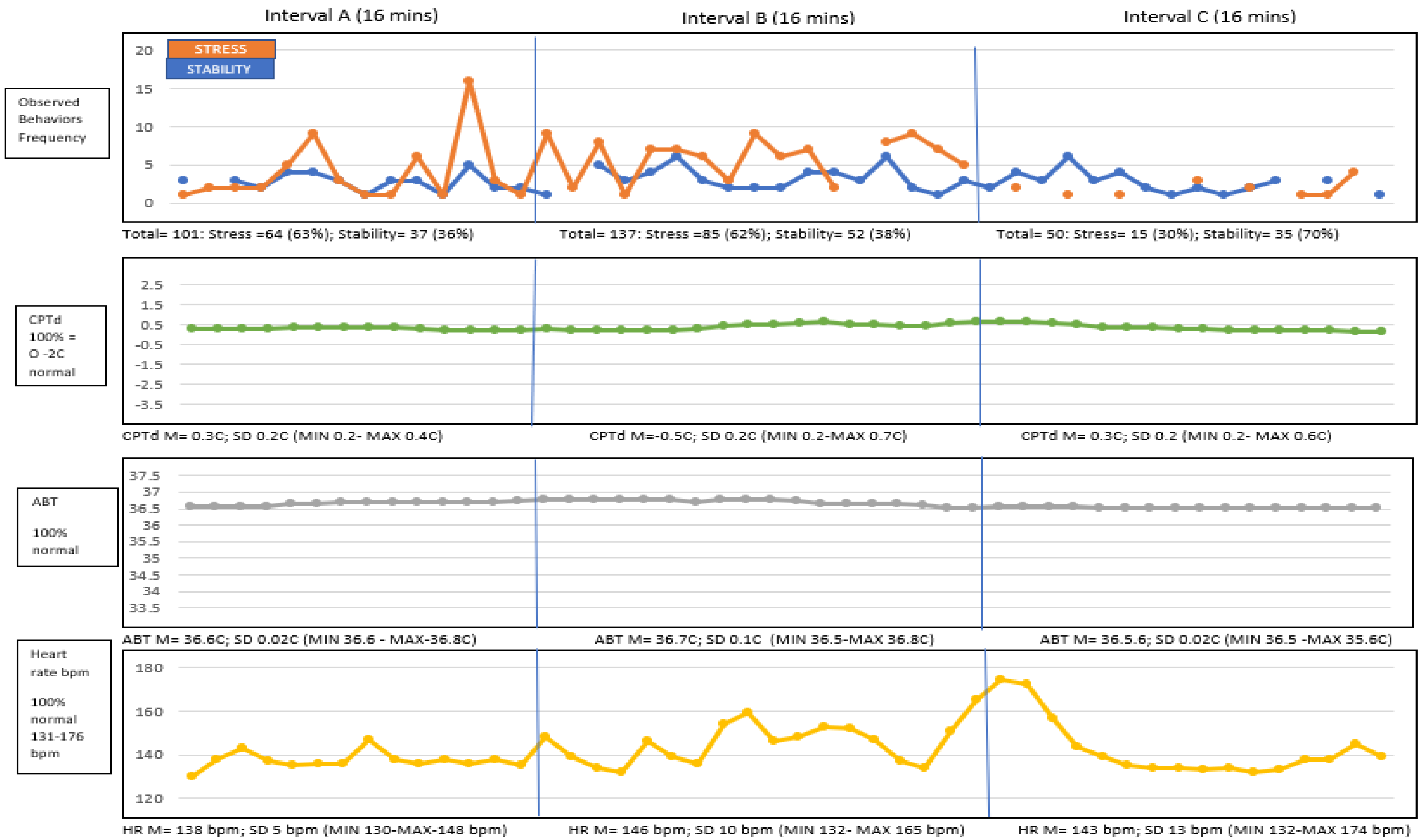

FIGURE A.17 OBSERVATION 17 COMBINED BEHAVIORAL AND PHYSIOLOGIC MEASURES

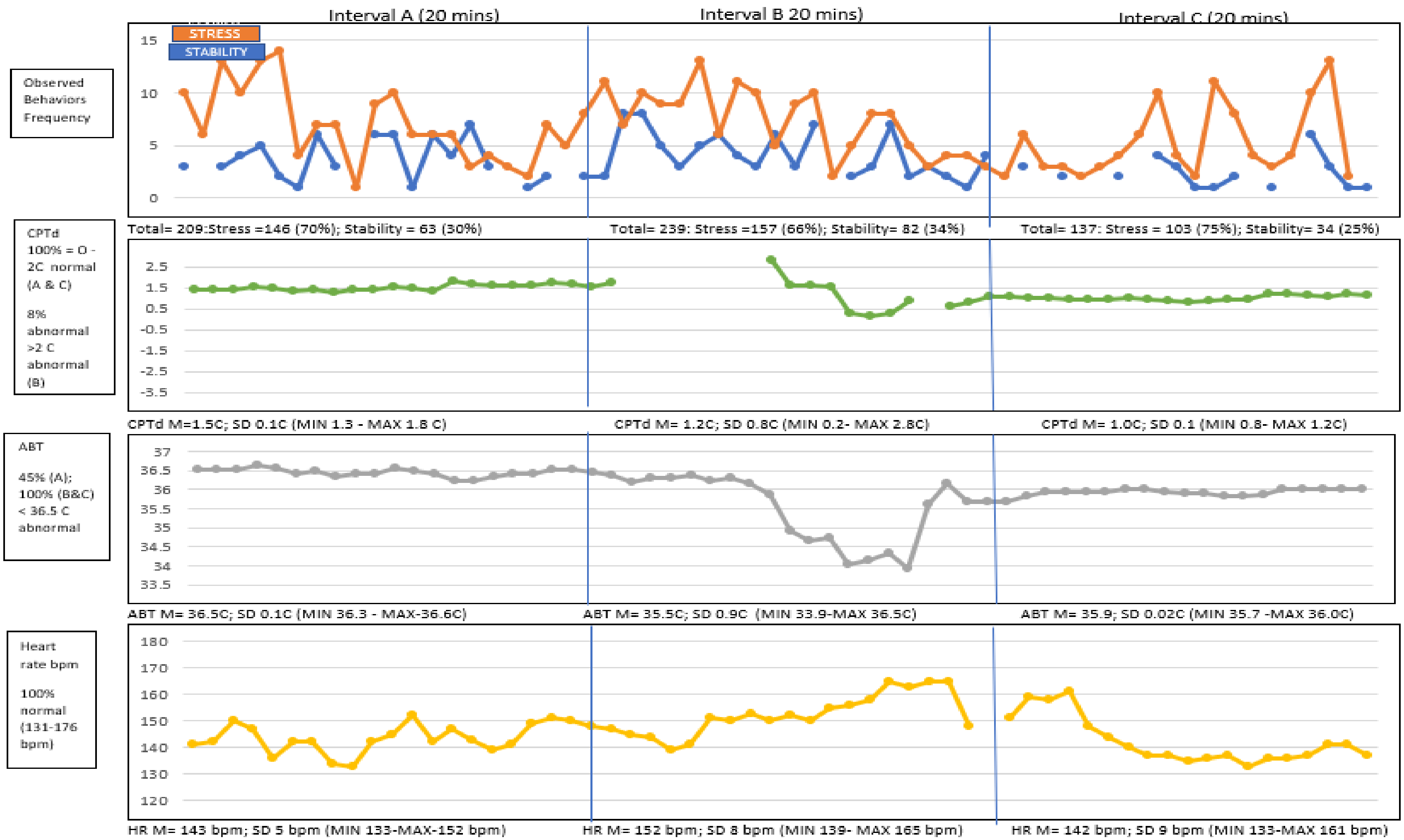

FIGURE A.18 OBSERVATION 18 COMBINED BEHAVIORAL AND PHYSIOLOGIC MEASURES

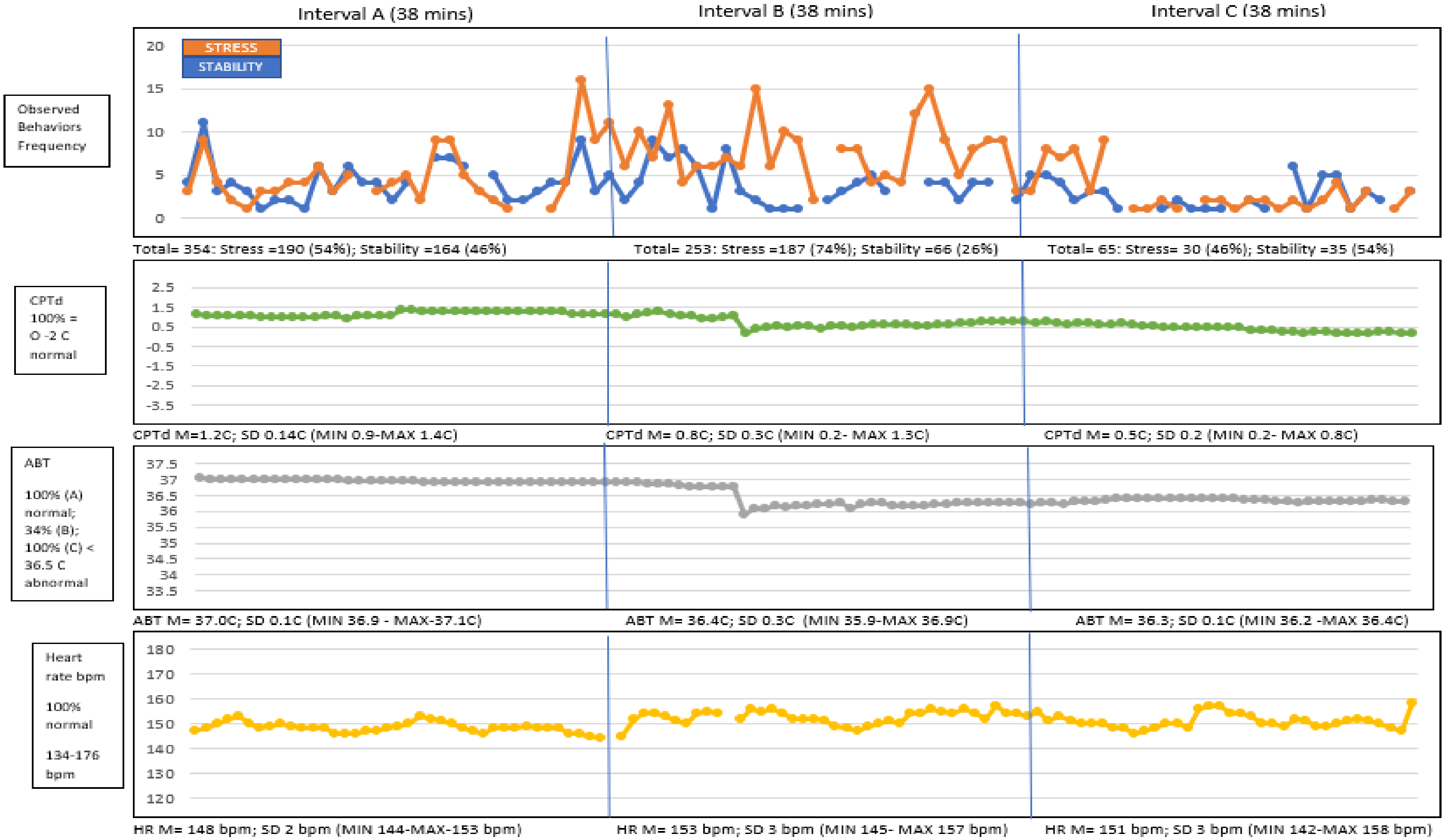

FIGURE A.19 OBSERVATION 19 COMBINED BEHAVIORAL AND PHYSIOLOGIC MEASURES

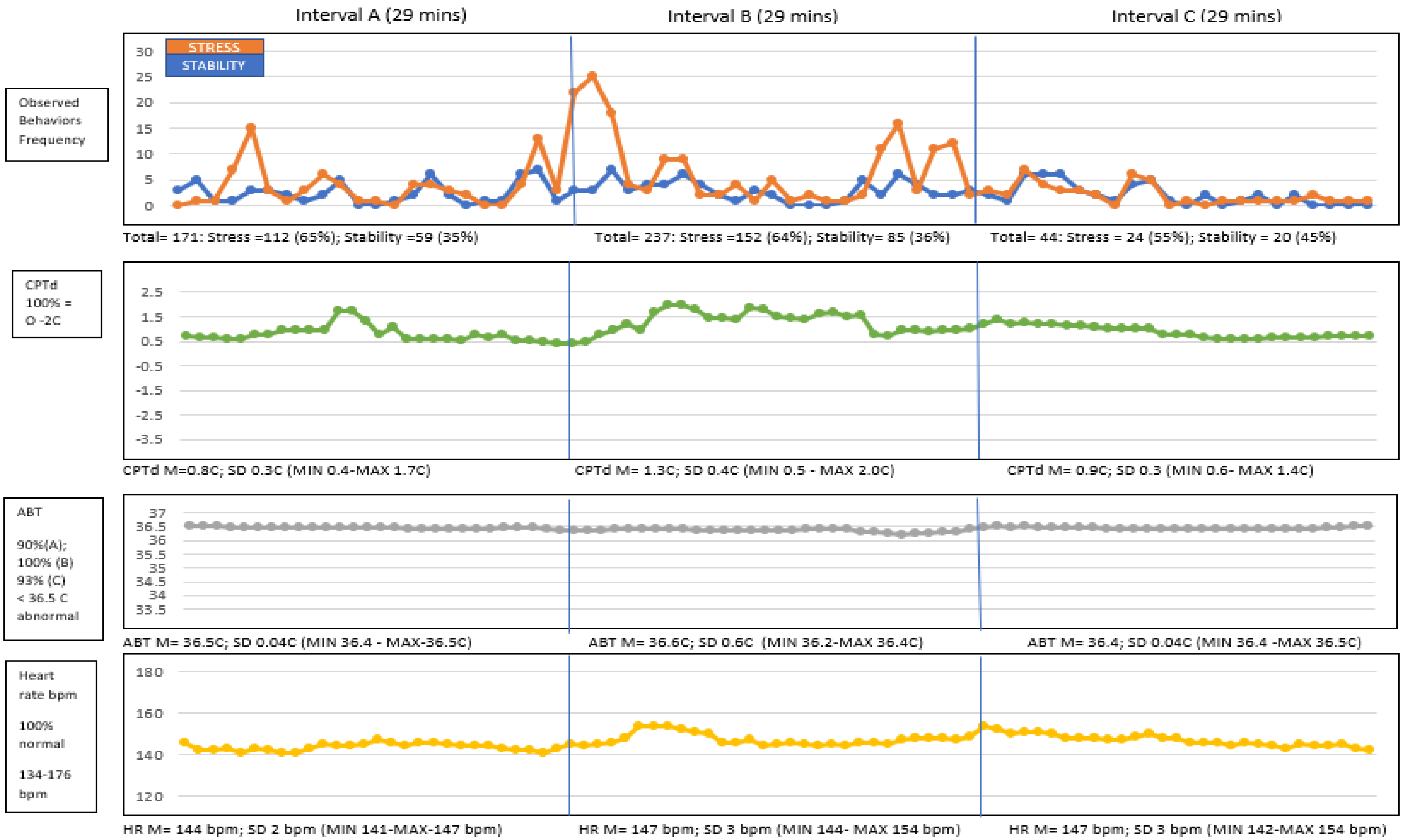

FIGURE A.20 OBSERVATION 20 COMBINED BEHAVIORAL AND PHYSIOLOGIC MEASURES